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Evaluation of Fibromyalgia Frequency in Chronic Urticaria Patients and Its Association with Urticaria Severity

Kronik Ürtiker Hastalarında Fibromiyalji Sendromu Sıklığının Değerlendirilmesi

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ÖZ

Amaç: Kronik ürtiker, nedeni tam olarak aydınlatılamamış kaşıntılı bir deri hastalığıdır. Otoimmünite ve psikojenik faktörlerin de patogenezde rolü olabileceği düşünülmektedir. Fibromiyalji sendromu (FMS) psikojenik nedenlerle ilişkili olabileceği düşünülen bir romatizmal hastalıktır. Çalışmamızda kronik ürtiker hastalarında FMS sıklığı ve şiddetini araştırmayı ve kronik ürtikere eşlik eden fibromiyalji varlığının klinik özelliklere ve dermatoloji yaşam kalitesine etkisini değerlendirmeyi planladık.
Araçlar ve Yöntem: Çalışmaya kronik ürtiker tanısı almış ve sistemik hastalık öyküsü olmayan 100 hasta, yaş ve cinsiyet açısından eşleştirilmiş 100 sağlıklı kontrol dahil edildi. Ürtiker şiddeti dermatoloji yaşam kalite indeksi skorları (DYKI) hesaplanarak değerlendirildi. Klinik şiddet ve fonksiyonel disabilite durumları vizuel analog skala (VAS) ve fibromiyalji etki anketi (FIQ) ile değerlendirildi.
Bulgular: Hasta grubunun yaş ortalaması 37.7±1.32, kontrol grubunun ise 40.7±11.2 olarak saptandı (p=0.09). Hasta grubundaki FMS sıklığı (%45) kontrol grubundan (%13) istatistiksel olarak anlamlı şekilde yüksekti (p=0.00). Kronik ürtiker süresi FMS'li hastalarda istatistiksel olarak anlamlı derecede yüksek bulundu(p=0.001). FIQ ve DLQI değerleri arasında istatistiksel olarak anlamlı korelasyon saptandı (p=0.019). Hasta ve kontrol grubunda FMS süreleri, VAS ve FIQ açısından istatistiksel olarak anlamlı fark saptanmadı (p=0.432, p=0.201, p=0.332).
Sonuç: Kronik ürtiker hastalarında FMS sıklığının artmış olduğunu görülmektedir. Bu sonuç kronik ürtiker patogenezindeki nöromediatörlerin kronik dönemdeki etkileriyle ilişkili olabilir.

Anahtar Kelimeler: fibromiyalji; kaşıntı; kronik ürtiker; nörojenik inflamasyon; yaşam kalitesi

ABSTRACT

Purpose: Chronic urticaria is a skin disease with unknown etiology. Autoimmunity and psychogenic factors have been suggested to play a role in pathogenesis. Fibromyalgia is a rheumatic disease that may be associated with psychogenic factors. The aim of the study was to determine the frequency and severity of fibromyalgia and the effect of fibromyalgia coexistence on clinical features and dermatology life quality index in urticaria patients.
Materials and Methods: One hundred patients with chronic urticaria and no history of any systemic disease and 100 age- and sex-matched healthy controls were included. Urticaria severity was evaluated by the dermatology life quality index (DLQI). Clinical severity and disability status were evaluated by the visual analog scale (VAS) and fibromyalgia impact questionnaire (FIQ).
Results: The mean age of the chronic urticaria patient group was 37.7±1.32, and that was 40.7±11.2 in the control group (p=0.09). Fibromyalgia frequency (45%) in the chronic urticaria group was significantly higher than in the control group (13%) (p=0.00). The duration of chronic urticaria was significantly higher in the patients with FMS than in the patients without FMS (p=0.001). There was a statistically significant correlation between FIQ and DLQI (p=0.019). No significant differences in terms of FMS durations, VAS, and FIQ values were detected between groups (p=0.432, p=0.201, p=0.332).
Conclusion: High frequency of fibromyalgia in chronic urticaria patients was found. This may be related to the chronic effect of neuromediators involved in chronic urticaria pathogenesis.

Keywords: chronic urticarial; fibromyalgia; neurogenic inflammation; pruritus; quality of life

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INTRODUCTION

Urticaria is a skin disease characterized by erythematous and edematous plaques. Chronic urticaria is a type of urticaria that lasts more than 6 weeks. Autoimmunity, drugs, infections, food, and malignancies have been proposed to play a role in the etiology of chronic urticaria.[1-3] In addition, psychogenic factors are also thought to play a role in chronic urticaria etiopathogenesis.[4]

Fibromyalgia syndrome (FMS) is a rheumatic disease characterized by widespread chronic pain and tender points in specific regions. FMS is more commonly seen in female patients. FMS and chronic urticaria show similarities since psychogenic factors play a role in the pathogenesis of both diseases.[5-7] Data revealing that neurogenic inflammation plays a role in the pathogenesis of both diseases exist.[8-10] Variable results have been obtained in the studies investigating the association between chronic urticaria and fibromyalgia. In some studies, the frequency of FMS in chronic urticaria patients was found to be higher than in healthy controls, while reports revealing that the frequency of FMS is not different from that of the normal population also exist.[11] The evaluation of chronic urticaria and FMS association is essential for the determination of the triggering factors and targeted mechanisms in urticaria treatment. In our study, we aimed to evaluate the effect of accompanying fibromyalgia on the clinical features of urticaria and dermatology life quality index by examining the frequency and severity of FMS in urticaria patients.

MATERIALS and METHODS

In this cross-sectional and controlled study, we included 100 chronic urticaria patients (31 male, 69 female) with disease duration of longer than 6 weeks and with no history of diabetes, malignancy, rheumatologic, endocrinological, cardiovascular, cerebrovascular, inflammatory disease and alcohol consumption and age and sex-matched 100 healthy controls (31 male, 69 female) were included. The patients who were previously diagnosed with FMS were not included. The patients diagnosed with depression and using antidepressant and anticonvulsant (gabapentin, pregabalin vs.) treatment were not included.

The demographic data of the patients, chronic urticaria and FMS durations, coexisting diseases and drug use were recorded. Before starting the study, ethics approval was obtained from the Clinical Research Ethics Committee of Ahi Evran University (Approval Date: 23.05.2017 Approval number: 2017-09/84). The study was conducted according to the Principles of the Helsinki Declaration. Food, drug, stress, and infections were questioned as triggering factors. Dermatology life quality index scores were calculated to detect urticaria severity. The Dermatology life quality index questionnaire is a life quality scale widely used in determining the severity of dermatologic diseases.[12,13] The validation of the Turkish version of the DLQI was performed by Ozturkcan et al.[13] There are ten questions with 4 possible answers related to the effect of the dermatological disease on the social and physical activities of the patient in the questionnaire. The questionnaire includes questions regarding symptoms and feelings, daily activities, leisure, work and school life, personal relationships, and treatment. The maximum value of Dermatology life quality index questionnaire scores is 30, and the minimum value is 0. The high values show low life quality.

In our study, VAS scale, which was developed by Price et al., was used to determine the pain severity related to FMS. In this scale, the severity of pain was determined as numbers between 0 and 10. The number 0 refers to no pain, 1-4 mild pain, 5-6 moderate pain, and 7-10 severe pain.[14,15]

All the patients were evaluated by a Physical Medicine and Rehabilitation specialist and diagnosed with FMS according to the 2010 ACR (American College of Rheumatology criteria).[16] The criteria consisted of the Widespread Pain Index (WPI), computed as the number of areas in which the patient felt pain in the last week, and a Symptom Severity Scale (SSS), in which, apart from the number of somatic symptoms in general, fatigue, waking unrefreshed and cognitive symptoms are considered cardinal symptoms in the diagnosis of FMS. To satisfy the 2010 criteria, patients have to meet: (1) WPI≥7 and SSS≥5 or WPI between 3–6 and SSS≥9; (2) presence of symptoms at a similar level for at least 3 months; and (3) absence of other disorders that would explain the pain.[16]

The patients who were diagnosed with FMS were examined for the severity of FMS. The clinical severity of FMS and functional disability were evaluated with a validated Turkish version of the Fibromyalgia Impact Questionnaire (FIQ)[17]. FIQ includes ten questions referring to pain severity, daytime fatigue, morning tiredness, stiffness, anxiety, and depression. Low scores point to the low effect of the disease.[17-18]

Statistical Analysis

The analysis of the obtained statistical data was performed with the SPSS version 21.0 software program (IBM Corp Armonk NY, USA). The sample size of the study was calculated with power analysis that was performed with G power 3.1.9.6 (Franz Faul, Universitat Kiel Germany). The minimum size of the total sample size was calculated to be 197 patients with power analysis in which w=0.20, power (1- beta)=0.80, degree of freedom =1, and the effect size was taken for the Chi-square test. Power analysis was performed for independent groups t-test when the effect size was taken as d=0.45, power (1- beta) was taken as=0.85, and the minimum sample size was calculated as 180 cases. In this study, when these minimum sample sizes were taken into consideration, the sample size was determined as 200 patients.

Categoric variables were stated as numbers and percentages, while numeric values were stated as mean±standard deviation, median, and minimum and maximum values. For comparison of categoric variables, the Chi-square test, for comparison of mean values, independent samples t-test, and for comparison of median values, Mann-Whitney U test was used. The Pearson correlation test was used to analyze the correlation between groups.

RESULTS

In our study, 100 chronic urticaria patients (31 male 69 female) and age and sex-matched healthy controls (31 male 69 female) were included. The mean age of the patients was detected as 37.7±1.32 and 40.7±11.2 in the control group. No statistical significance was detected between groups in terms of age and sex (p=0.09, p=1.00, respectively). Gastritis was present in 8 patients, allergic rhinitis in 12 patients, asthma in 5 patients, and vertigo in 5 patients. As triggering factors, stress was detected in 77(77%) of the patients, food in 17(17%), and infections in 5(5%) patients (3 patients with upper respiratory tract infections. In 2 patients, urinary infections and in 3 patients (3%), drug use were found to be associated with chronic urticaria. 2 patients were using amoxicillin-clavulanic acid, 1 patient was using lansoprazole.

In the patient group, 45(45%) patients and 13(13%) cases in the control group were diagnosed with FMS. In the patient group, FMS frequency was statistically significantly higher than in the control group (p=0.00). In the patient group, the majority of the patients diagnosed with FMS were composed of female patients (n=34, 75.5%). Similarly, the majority of the patients diagnosed with FMS in the control group were composed of female patients (n=12, 92.3%). In the patient group, urticaria duration was 27.9±5.1 months, while FMS duration was 28.7±3.59 months. No significant difference in terms of FMS and urticaria duration was detected (p=0.902). In the control group, the duration of FMS was detected as 33.0±2.61 months, and no statistically significant difference in terms of FMS was detected between groups (p=0.432). The mean value of the FIQ score was detected as 42.3±2.82 and 49.1±6.05 in the patient and the control group, respectively (Table 1). The median value of VAS score in the patient group was 7(3-10) and 5(2-10) in the control group. No statistically significant difference was detected in terms of FIQ and VAS scores between groups (p=0.332, p= 0.201) (Table 1). There was a statistically significant correlation between FIQ and DLQI values (p=0.019).

When patients with FMS and without FMS in the study group were compared, the mean age of the patients with FMS was 40.5±13.31, while patients without FMS were 35.4±12.71. No significant difference between DLQI values of patients with FMS and without FMS was detected (p=0.763). No significant difference between the mean age values was detected between groups (p=0.057). No significant difference in gender distribution was found between patients with FMS and without FMS groups (p=0.097). Chronic urticaria duration in patients with FMS group was 40.0±46.3 months and 16.76±16.70 months in patients without FMS group. Chronic urticaria duration in patients

with FMS group was significantly higher than in patients without FMS group (p=0.001) (Table 2).

Tablo 1. Demographic and clinical characteristics of patient and control groups

Variables	Patient group	Control group	p
Age	37.7±1.32	40.7 ±11.2	0.090
FMS cases	45	13	0.000
Chronic urticaria duration (months)	27.9±5.1	-	
FMS duration (months)	28.7±3.59	33.0±2.61	0.432
DLQI	10.41±0.70	-	
FIQ	42.3±2.82	49.1±6.05	0.332
VAS	7 (3-10)	5 (2-10)	0.201

DLQI: Dermatology life quality index, FIQ: Fibromyalgia impact questionnaire, VAS: Visual analog scale, p<0.05 was accepted as statistically significant

Table 2. Demographic and clinical characteristics of the patients with FMS and the patients with and without FMS in chronic urticaria patient groups

Variables	The patients with FMS	The patients without FMS	p-value
Age	40.5±13.31	35.4±12.71	0.057
Gender			
Female	34	33	0.097
Male	11	22	
Chronic urticaria duration	40.0±46.3	16.76±16.70	0.001
DLQI	10.64±6.87	10.22±7.03	0.763

DLQI: Dermatology life quality index, p<0.05 was considered statistically significant

DISCUSSION

Chronic urticaria and FMS are clinical conditions whose etiopathogenesis has not been completely elucidated yet. Chronic urticaria has been shown to coexist with various stress-related diseases. Psychosocial, behavioral, and neurobiological factors have been suggested to play a role in FMS development.[19] Increased frequency of some skin diseases have been reported in FMS patients. In a study by Erdogan et al., the frequency of xerosis, dermographism, lichen simplex chronicus, neurotic excoriation, and seborrheic dermatitis and pruritus, burning and stinging sensation were reported to be higher in FMS patients.[20]

Neuroinflammation is thought to play a role in the etiology of chronic urticaria and FMS. This suggests a close relationship between chronic urticaria and FMS.[21-27] There are some studies that reveal an increased frequency of FMS in chronic urticaria patients, while studies suggesting no difference in the frequency of FMS compared to normal population also exist.[5-7,11] In our study, the frequency of FMS in the chronic urticaria patient group (45%) was statistically significantly higher than in the control group (13%). This frequency was higher than those in Mathkor et al. (%34.1) and Oktayoğlu et al. (%32.5) but lower than in Toressani et al. (70%) [5-7] Toressani et al. stated that this result was unexpectedly high as the frequency of fibromyalgia was 2.2% in the general population. It is also notable that the frequency of fibromyalgia in the control group was higher than in the study of Toressani et al. This result may be related to different geographic and demographic characteristics of the study population.

Torresani et al. reported that FMS-related symptoms, such as pain, started before the initiation of urticaria, and this suggests that chronic urticaria development may be the result of neurogenic inflammation in FMS.[6] Differing from the study by Torresani et al., no statistically significant difference was detected between chronic urticaria and FMS durations in chronic urticaria patients. The result that no significant difference was detected in FMS durations between the patient and the control groups reveals that the presence of chronic urticaria is not a risk factor for early development of FMS compared to healthy controls. In a study by Gözübüyükoğulları et al. Chronic urticaria durations in the patients with FMS were foud to be higher than in the patients without FMS, but this was not statistically significant. Contrary to this study, the finding that chronic urticaria duration in the patients with FMS was significantly higher than in the patients without FMS may result from the high number of cases in the control group. This result suggests that the long-term effect of the mediators playing a role in chronic urticaria may also play a role in the development of FMS. The finding that there is no significant difference in the DLQI values in the patients with and without FMS suggests that the severity of chronic urticaria is not higher in the patients with FMS. In our study, similar to that of Gözübüyükoğulları et al., no significant difference between the mean age values of the patients with and without FMS was detected. This finding suggests that age does not affect the development of FMS.

Autoimmunity is a condition that accompanies both chronic urticaria and FMS. Especially chronic inflammatory diseases such as SLE are commonly seen in both diseases.[29-31] Gözübüyükoğulları et al. reported that the patients with FMS had a higher percentage of thyroid autoimmunity than the patients without FMS, but the results were not statistically significant. In our study, the presence

of chronic inflammatory disease was taken as an exclusion criterion, and autologous serum skin test and thyroid autoimmunity were not evaluated.

Similar to the study of Yener et al., the detection of correlation between FIQ and DLQI suggests that common pathogenetic pathways play a role in both diseases.[32] Yener et al. reported higher FIQ and VAS values in chronic urticaria patients than in healthy controls. In our study, the fact that no difference was detected between FIQ and VAS values between groups reveals that the presence of chronic urticaria does not cause an increase in the severity of FMS.

The limitations of the study include a small number of patients in a rural region and the absence of an evaluation of autologous serum skin test and thyroid antibodies. Also, specific scales such as the Pittsburgh sleep quality index, which measures sleep quality and sleep disturbance, and the Multidimensional Assessment of Fatigue (MAF) scale were not used.[33] In addition, anxiety and depression were not examined. The absence of an evaluation of distress with anxiety and depression scales is also among the limitations of the study.

In conclusion, the results obtained in our study revealed that the frequency of FMS in chronic urticaria is higher than in healthy controls. These findings are in line with the literature. FMS development in chronic urticaria patients may be related to the chronic term effects of neuromediators in chronic urticaria. The triggering of the diseases with psychogenic factors and the role of neuroinflammation in etiopathogenesis suggest that chronic urticaria and FMS are closely related. Further studies investigating the association between chronic urticaria and FMS are warranted.

Conflict of Interest

The authors declare that there is not any conflict of interest regarding the publication of this manuscript.

Ethics Committee Permission

Before starting the study, approval was obtained from the Clinical Research Ethics Committee of Ahi Evran University (Approval Date: 23.05.2017 Approval number: 2017-09/84).

Authors' Contributions

Concept/Design: EMA, SŞ. Data Collection and/or Processing: EMA, SŞ. Data analysis and interpretation: EMA, SŞ. Literature Search: EMA, SŞ. Drafting manuscript: EMA. Critical revision of manuscript: SŞ, EMA. Supervision: SŞ.

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