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ÖZGÜN MAKALE / ORIGINAL ARTICLE

Investigation of Pathergy In Patients With Fibromyalgia*

Fibromiyaljili Hastalarda Paterji Pozitifliğinin Araştırılması

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ABSTRACT

Aim: Recent studies showed increased axon reflex flare reaction to mechanical and chemical stimuli associated with neurogenic inflammation in patients with fibromyalgia (FM). Pathergy test is identified as a non-specific hypersensitivity reaction to minimal trauma. The purpose of this study was to investigate whether patients with FM had a positive pathergy test or not.

Methods: Forty-six patients who met the 1990 American College of Rheumatology (ACR) criteria for the classification of FM and fifty-one healthy control subjects (HCs) were included in this study. Twenty-eight patients with Behcet's disease were included as disease control for Pathergy test. The Fibromyalgia Impact Questionnaire (FIQ) was used for assessment of functional status in patients with FM. The Nottingham Health Profile was used for assessment of quality of life in all subjects.

Results: There was no significant difference in demographic characteristics between the three groups ($p > 0.05$). NHP-pain, NHP-physical mobility, NHP-energy, NHP-emotional reaction, NHP-sleep and NHP-total scores were significantly higher in patients with FM compared to HCs ($p < 0.001$). Neither patients with FM nor HCs had a positive pathergy test.

Conclusion: There are some pathophysiological changes in the skin biopsies of patients with FM; however, these changes are not accompanied by a positive pathergy test.

Key Words: Fibromyalgia, Pathergy test

ÖZET

Amaç: Son çalışmalar fibromiyalji (FM) hastalarında mekanik ve kimyasal uyarılara bağlı olarak oluşan nörojenik inflamasyonla beraber artmış aksonal refleks varlığını ortaya koymuştur. Paterji testi derinin minimal bir travmaya karşı gösterdiği nonspesifik hipersensitivite reaksiyonu olarak tanımlanmaktadır. Bu çalışmada amaç, FM'li hastalarda Paterji testinin pozitif olup olmadığının araştırılmasıdır.

Yöntem: Amerikan Romatizma Cemiyeti Sınıflandırma kriterlerine göre FM tanısı alan 46 hasta ve 51 sağlıklı kontrol çalışmaya dahil edilmiştir. Yirmi sekiz behçet hastası da paterji açısından hastalıklı kontrol olarak çalışmaya alınmıştır. Fonksiyonel durum Fibromiyalji Etki Skalası ile, yaşam kalitesi Nottingham Sağlık Profili anketiyle değerlendirilmiştir.

Bulgular: Demografik özellikler açısından üç grup arasında anlamlı bir farklılık bulunmadı ($p>0.05$). NHP-ağrı, NHP-fiziksel mobilite, NHP-yorgunluk, NHP-emosyonel durum, NHP-uyku and NHP-total skorları FM'li hasta grubunda kontrol grubuna göre anlamlı olarak yüksek bulundu ($p<0.001$). FM'li hasta ve sağlıklı kontrollerin hiçbirinde paterji pozitifliği saptanmadı.

Sonuç: FM hastaların cilt biyopsilerinde her ne kadar patofizyolojik değişiklikler olsa da bu değişikliklere paterji testi pozitifliği eşlik etmemektedir.

Anahtar Kelimeler: Fibromiyalji, Paterji

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INTRODUCTION

Fibromyalgia (FM) is a chronic generalized pain condition with tender points which can be found in physical examination. It brings about a number of symptoms such as fatigue, headache, and irritable bowel syndrome and sleep disturbance (1, 2). Several studies were conducted on dermal involvement in patients with fibromyalgia. These studies showed increased axon reflex flare reaction to mechanical and chemical stimuli and lower threshold for capsaicin-induced flare inpatients with FM, which was reported to be associated

with increased neurogenic inflammation (3). Pathergy is a non-specific hypersensitivity reaction to minimal trauma. Skin pathergy test is one of the minor diagnostic criteria for Behcet's disease (4). This test was also shown to be positive in pyoderma gangrenosum and Sweet's syndrome. Underlying causes of a positive pathergy test are still unknown. In the present study, we aimed at investigating whether patients with FM had a positive pathergy test or not.

MATERIALS and METHODS

Forty-six patients (38 females and 8 males) who met the 1990 American College of Rheumatology (ACR) (1) criteria for the classification of FM and fifty-one (40 females and 11 males) sex and age matched healthy control subjects (HCs) were included to this study. Twenty-eight (20 females and 8 males) sex and age matched patients who fulfilled the International Study Group Classification Criteria (4) for Behcet's disease were included as disease control group for Pathergy test. Demographics, duration of disease and medications used were noted. Individuals with rheumatic or dermatological diseases and persons who were administered systemic corticosteroids or any other immunosuppressants within the last 3 months in FM and HCs group were excluded from the study. Persons with a history of tumor necrosis factor alpha inhibitors or patients who received immunosuppressive agents or systemic steroids >7.5 mg/kg within 4 weeks before the time of study entry were excluded in patients with Behcet's disease. Control subjects consisted of healthy people without clinical evidence of rheumatic diseases or any other systemic disorders. The Fibromyalgia Impact Questionnaire (FIQ) (5, 6) was used for assessment of disease severity and functional status in patients with FM. In addition, The Nottingham Health Profile (NHP) was used for assessment of quality of life in all subjects (7, 8). Pathergy test was administrated by the same dermatologist to all subjects. The skin was not cleaned with antiseptic solution. A 21-gauge hypodermic needle was inserted into the dermis through the forearm skin at an angle of 30º to a depth of 1.5-2 mm. Each subject had four needle pricks. The test results were checked at hours 24 and 48 by using a three-point-scale where the results meant as follows: 0=needle mark only, 1+= papule only, and 2+=pustule. The test results were considered positive when at least one site scored 2+ at hours 24 and 48 following intradermal needle prick (9).

Statistical analysis

Data were expressed as mean ± standard deviation (SD). Differences in variables between the groups were analyzed by using Student's t test and One-way Anova. Frequency differences between categorical groups were analyzed by using Chi-square test. A p value smaller than 0.05 was considered statistically significant. All analyses were performed in Statistical Package for Social Sciences software version 18.0 for Windows.

RESULTS

Neither patients with FM nor healthy control subjects had a positive pathergy test. 11 of 28 patients with Behcet's disease had positive Pathergy test. The mean age of patients with FM and HCs was 35.6 ± 11.2 years and 37.1 ± 12.3 years, respectively. There was no

significant difference in demographic characteristics between the three groups (p > 0.05) (Table 1). The mean duration of disease was 3.4 ± 2.8 years, and the mean tender point count was 14 ± 2. In addition, the mean FIQ score was 51.41 ± 17.30 in patients with FM (Table II). NHP-pain, NHP-physical mobility, NHP-energy, NHP-emotional reaction, NHP-sleep and NHP-total scores were significantly higher in patients with FM compared to HCs (p <0.001) (Table 2). NHP-social isolation score was also higher in FM group compared to HC group (p = 0.024).

Table 1. Demographic characteristics of patients with FM, HCs and BD

	Patients with FM (mean±SD)	HCs (mean±SD)	BD(mean±SD)	p
BMI (kg/m²)	25.53±4.36	24.63±4.67	26.0±5.9	NS
Age (year)	35.6±11.2	37.1±12.3	36.8±14.1	NS
Gender (female/male)	38/8	40/11	20/8	NS

BMI= Body Mass Index, FM= Fibromyalgia, HCs= Healthy Control Subjects, BD=Behcet's disease, SD= Standard Deviation, NS= Not significant in t and chi-square tests

Table 2. Clinical characteristics of patients with FM and HCs

	Fibromyalgia (mean±SD)	Control (mean±SD)	P
Duration of disease (year)	3.4±2.8	-	-
Tender point count	14±2	5±2	< 0.001
FIQ	51.41±17.30	12.82±14.80	< 0.001
NHP-pain	71.66±28.21	24.68±28.65	< 0.001
NHP-physical mobility	48.32±20.08	20.34±21.78	< 0.001
NHP-energy	67.38±32.58	28.35±28.98	< 0.001
NHP-emotional reaction	50.54±29.02	20.12±26.14	< 0.001
NHP-social isolation	26.95±32.98	13.15±26.11	0.024
NHP-sleep	42.99±32.33	15.45±23.92	< 0.001
NHP-total	50.49±20.57	19.70±19.41	< 0.001

NHP= Nottingham Health Profile, FIQ= Fibromyalgia Impact Questionnaire, SD=Standard Deviation

DISCUSSION

There are several studies in the literature assessing the skin involvement in patients with FM. These studies showed that FM accounted for a malfunction in the descending anti-nociceptive pathways. They also showed specific receptors and characteristic electron microscopic findings as well as increased axon reflex flare reaction to mechanical and chemical

stimuli and lower threshold of capsaicin-induced flare in the skin biopsies of patients with FM (10).

Kim et al. reported increased N-methyl-D-aspartate receptor subtype 2D expression in the skin of patients with FM (11). Some other authors detected IL-1β and TNF-α immunoreactivity in the tissues of patients with FM which could not be found in the healthy control skin. They pointed out that neurogenic inflammation occurred in the skin of patients with FM (12).

In another study, an increased number of mast cells were found in the papillary dermis of patients with FM (13). In the light of all these findings, we aimed at investigating whether patients with FM had a positive pathergy test or not.

Pathergy is hyper-reactivity of the skin to minimal trauma. A positive pathergy test is one of the minor diagnostic criteria for Behcet's disease. Pathergy test is also known to be positive in pyoderma gangrenosum and other neutrophilic dermatoses such as Sweet's syndrome (14). It was shown to be positive in up to 84% of Turkish patients with Behcet's disease (15). On the other hand, there are only a limited number of studies investigating the pathergy in patients with rheumatic diseases. In the present study, none of the patients with FM had a positive pathergy test. Aydin et al. also investigated the pathergy in patients with Familial Mediterranean fever and found that none of the patients had a positive pathergy test (16). Despite the negative test results, patients with FM experienced decreased quality of life in this study. In addition, the NHP sub-scores increased with decreased quality of life in patients with FM.

There are only a limited number of studies assessing the quality of life by using NHP in patients with FM. Dogan et al. (17) used NHP for assessment of quality of life in patients with FM and found that patients with FM scored higher in all NHP sub-items (save for NHP-social isolation and NHP-emotional reaction) compared to control subjects.

In conclusion, some pathophysiological changes occur in the skin of patients with FM; however, these changes are not accompanied by a positive pathergy test.

REFERENCES

1. Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, Tugwell P, Campbell SM, Abeles M, Clark P, Fam AG, Farber SJ, Flechtner JJ, Franklin CM, Gatter RA, Hamaty D, Lessard Jichtbroun AS, Masi AT, McCain GA, Reynolds WJ, Romano TJ, Russell IJ, Sheon RP. The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee. Arthritis Rheum. 1990; 33(2):160-72
2. Clauw DJ. The pathogenesis of chronic pain and fatigue syndromes, with special reference to fibromyalgia. Med Hypotheses. 1995; 44(5):369-78
3. Torresani C, Bellafiore S, De Panfilis G. Chronic urticaria is usually associated with fibromyalgia syndrome. Acta Derm Venereol. 2009; 89(4):389-92
4. ISGfB. Criteria for diagnosis of Behçet's disease. International Study Group for Behçet's Disease. Lancet. 1990; 335(8697):1078-80
5. Burckhardt CS, Clark SR, Bennett RM. The fibromyalgia impact questionnaire: development and validation. J Rheumatol. 1991; 18: 728-733
6. Sarmer S, Ergin S, Yavuzer G. The validity and reliability of the Turkish version of the fibromyalgia impact questionnaire. Rheumatol Int. 2000; 20: 9-12
7. Hunt SM, McKenna SP, McEwen J, Williams J, Papp E. The Nottingham Health Profile: subjective health status and medical consultations. Soc Sci Med A. 1981; 15: 221-9.
8. Kucukdeveci AA, McKenna SP, Kutlay S, Gursel Y, Whalley D, Arasil T. The development and psychometric assessment of the Turkish version of the Nottingham health profile. Int J Rehabil Res. 2000; 23: 31-38
9. Baker R.B. Smith EV, Osheik AS. Pathergy test. Practical Neurology. 2011; 11:301-302
10. Kim SH. Skin biopsy findings: Implications for the pathophysiology of fibromyalgia. Med Hypotheses. 2007; 69:141-144
11. Kim SH, Kim DH, Oh DH, Clauw DJ. Characteristic electron microscopic findings in the skin of patients with fibromyalgia--preliminary study. Clin Rheumatol. 2008; 27(3):407-11
12. Salemi S, Rethage J, Wollina U, Michel BA, Gay RE, Gay S, Sprott H. Detection of interleukin 1beta (IL-1beta), IL-6, and tumor necrosis factor-alpha in skin of patients with fibromyalgia. J Rheumatol. 2003; 30(1):146-50
13. Blanco I, Béritze N, Argüelles M, Cárcaba V, Fernández F, Janciauskiene S, Oikonomopoulou K, de Serres FJ, Fernández-Bustillo E, Hollenberg MD. Abnormal overexpression of mastocytes in skin biopsies of fibromyalgia patients Clin Rheumatol. 2010; 29(12):1403-12.
14. Varol A, Seifert O, Anderson CD. The skin pathergy test: innately useful? Arch Dermatol Res. 2010; 302(3):155-68.
15. Tüzün Y, Yazici H, Pazarli H, Yalçin B, Yurdakul S, Müftüoğlu A. The usefulness of the nonspecific skin hyperreactivity (the pathergy test) in Behçet's disease in Turkey. Acta Derm Venereol. 1979; 59(1):77-9.
16. Aydin F, Akpolat T, Senturk N, Bagci H, Yasar Turanli A. Evaluation of pathergy test positivity in familial Mediterranean fever patients and comparison of clinical manifestations of FMF with Behçet's disease. 2009; 28(11):1331-5.
17. Dogan SK, Aytur YK, Atbasoglu C. Assessment of the relatives or spouses cohabiting with the fibromyalgia patients: is there a link regarding fibromyalgia symptoms, quality of life, general health and psychologic status? Rheumatol Int. 2011; 31(9):1137-4