

Evaluation of Sympathetic Skin Response and F Wave in Fibromyalgia Syndrome Patients

Fibromiyalji Sendromlu Hastalarda Sempatik Deri Yanıtı ve F Dalgasının Değerlendirilmesi

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Objectives: This study was planned to perform an electroneuromyographic evaluation of the sympathetic skin response (SSR) and F wave in order to determine whether there is an autonomic dysfunction in fibromyalgia syndrome (FMS).

Patients and methods: Thirty-eight patients (1 male, 37 females; mean age 40.6±9.6; range 22 to 60 years) who were admitted to our clinic between March 2005 and March 2006 and diagnosed with FMS and 30 healthy controls (1 male, 29 females; mean age 39.5±9.0 years; range 22 to 55 years) were enrolled in this study. After clinical examination, all patients were evaluated in the electroneuromyography (ENMG) laboratory with respect to SSR and F wave. The F wave was measured in both median and ulnar nerves. The SSR was evaluated in the median nerve. Patients were assessed with respect to the mean value of the F wave distal latency, the distal latency for SSR and the amplitude values. All patients were also evaluated for pain (Visual analogue scale, VAS), number of tender points (NTP), depression (Beck depression inventory, BDI) and functional capacity (fibromyalgia impact questionnaire, FIQ).

Results: No statistically significant difference was found in the distal latency values of the F wave between the groups ($p>0.05$). Fibromyalgia syndrome patients were found to have significantly higher SSR amplitude values and lower latency values for both sides when compared with controls ($p<0.05$). No statistically significant correlation was found between the SSR (amplitude and latency), and F wave results and the VAS, BDI, FIQ and NTP scores in the patients with FMS ($p>0.05$).

Conclusion: Our results support that, in the sympathetic nervous system of the patients with FMS, there is an alteration that shows the presence of autonomic dysfunction.

Key words: Autonomic dysfunction; F-wave; fibromyalgia; sympathetic skin response.

Amaç: Bu çalışmada, fibromiyalji sendromu (FMS)'nda otonomik disfonksiyon mevcut olup olmadığının belirlenmesi amacıyla sempatik deri yanıtı (SDY) ve F dalgasının elektronöromiyografik incelenmesi planlandı.

Hastalar ve yöntemler: Mart 2005 - Mart 2006 tarihleri arasında kliniğimize başvuran ve fibromiyalji sendromu tanısı konulan 38 hasta (1 erkek, 37 kadın; ort. yaş 40.6±9.6 yıl; dağılım 22-60 yıl) ve 30 sağlıklı kontrol (1 erkek, 29 kadın; ort. yaş 39.5±9.0 yıl; dağılım 22-55 yıl) çalışmaya dahil edildi. Klinik inceleme sonrasında tüm hastalar elektronöromiyografi (ENMG) laboratuvarında SDY ve F dalgası açısından değerlendirildi. F dalgası hem median hem de ulnar sinirden ölçüldü. Sempatik deri yanıtı median sinirden değerlendirildi. Hastalar F dalga distal latans ortalaması, SDY distal latans değeri ve amplitüd değerleri açısından değerlendirildi. Tüm hastalar ağrı (görsel analog skalası, GAS), hassas nokta sayısı (HNS), depresyon (Beck depresyon envanteri, BDE) ve fonksiyonel kapasite (fibromiyalji etkisi anketi, FEA) açısından da değerlendirildi.

Bulgular: Gruplar arasında F dalgası distal latans değerleri açısından istatistiksel olarak anlamlı herhangi bir fark bulunmadı ($p>0.05$). Kontrol grubu ile karşılaştırıldığında FMS'li hastaların her iki tarafta da daha yüksek SDY amplitüdü değerlerine ve daha düşük latans değerlerine sahip olduğu tespit edildi ($p<0.05$). Fibromiyalji sendromlu hastalarda SDY (amplitude ve latans) ve F dalgası sonuçları ile GAS, BDE, FEA ve HNS skorları arasında istatistiksel olarak anlamlı herhangi bir korelasyon tespit edilmedi ($p>0.05$).

Sonuç: Sonuçlarımız FMS'li hastaların sempatik sinir sisteminde otonom disfonksiyonu gösteren bir değişiklik olduğunu desteklemektedir.

Anahtar sözcükler: Otonom disfonksiyon; F-dalgası; fibromiyalji; sempatik deri yanıtı.

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Fibromyalgia syndrome (FMS) is a chronic disorder which is characterized by diffuse, widespread pain and the presence of tender points.^[1] Various etiologies have been proposed for FMS, but the etiology and pathophysiologic mechanism for diffuse pain is still unknown.

It is possible that several phenomena may play overlapping roles in the development of the syndrome and one of these may be autonomic nervous system (ANS) dysfunction.^[2] Pain is the major symptom, and recent studies have considered this to be neuropathic pain related to central nervous system sensitization.^[3] Studies have also shown the association of this pain with sympathetic neurotransmitters and increased function in the sympathetic nervous system of FMS patients.^[4-6] Stress response plays an important role in the symptoms, and it is believed that the ANS has a close relationship with the efficiency of the stress response and the hypothalamic-pituitary-adrenal axis (HPA).^[7]

A simple and reliable neurophysiologic method to evaluate the ANS is the study of the sympathetic skin response (SSR).^[8,9] Using an electrical stimulation, the eccrine sweat glands of the skin are activated via a reflex loop which includes large, myelinated sensory fibers, central synapses and efferent sympathetic pre- and post-ganglionic nerve fibers.^[9]

Fibromyalgia syndrome has complex symptoms and the role of the peripheral nervous system (PNS) in these is not yet clear. Only a few studies have described abnormal electrodiagnostic test results.^[10] F wave is a late response recorded from the muscle elicited by an electric impulse conveyed antidromically to alpha-motor neurons in the spinal cord. F wave latency and frequency are assessed to provide information about the proximal segment conduction of the nerves.^[11] In this study, F wave is investigated to determine whether the PNS has been affected in FMS.

This study was designed to investigate the electroneuromyographic (ENMG) evaluation of the SSR and F wave in FMS and their correlation with clinical outcomes.

PATIENTS AND METHODS

The fibromyalgia syndrome group was recruited from the patients admitted to the Physical Medicine and Rehabilitation (PMR) outpatient clinic between March 2005 and March 2006 with widespread musculoskeletal pain. Among 68 patients, 38 (1 male, 37 females; mean age 40.6±9.6 years; range 22 to 60 years) meeting the

1990 American College of Rheumatology classification criteria for FMS were enrolled in this study. The control group included 30 healthy volunteers (1 male, 29 females; mean age 39.5±9.0; range 22 to 55 years). A total of 75 healthy subjects were screened over a one year period. Fifty subjects without musculoskeletal pain complaint and with no disabling coexisting diseases were eligible for the study. Most of them were accompanying persons of the patients. They were informed about the research, and 20 of them did not approve electrodiagnostics tests. Thirty healthy controls gave written consent and enrolled in this study. After a physical examination, routine laboratory investigations including full blood count, erythrocyte sedimentation rate (ESR) and biochemical markers were carried out. Exclusion criteria for this study were entrapment neuropathies-polynuropathies (based on electrodiagnostic tests), malignancy, diabetes mellitus, chronic renal failure, and inflammatory joint disease. None of the patients was under medication such as tricyclic antidepressants, muscle relaxants or analgesics for at least four weeks before therapy.

Clinical assessment

The number of tender points (NTP), pain, depression and functional capacity of the patients were evaluated. Tender points were determined by an algometer (Greenwich, USA). Pain was assessed using a 10 cm visual analog scale (VAS) where 0 corresponded to no pain and 10 to the worst pain. Functional capacity was evaluated by the fibromyalgia impact questionnaire (FIQ) which is a self-administered questionnaire consisting of 10 criteria, including physical function, work status, anxiety, pain, fatigue, sleep, depression, stiffness and well-being. It has different scores for each item and a final calculation was done on a maximum score of 100.^[12] Beck's depression inventory (BDI) was used to evaluate the level of depression. It is also a self-administered questionnaire and consists of 21 items with a range of 0-63 where higher scores indicate major depression.^[13]

Electrodiagnostic testing

After clinical examination, all patients were investigated in an ENMG laboratory by means of SSR and F wave. All electrodiagnostic tests were performed by using a Neuropack MEB-2200 Nihon Kohden ENMG apparatus at a room temperature of 26 °C. Before testing, and patients were informed about taking a restful sleep, stopping coffee and alcohol intake.

F wave studies were performed for median and ulnar nerves bilaterally. The active electrode was placed over

the middle of the muscle belly of the abductor pollicis brevis for the median nerve and the abductor digiti minimi for the ulnar nerve. The reference electrodes were placed distally. F waves were recorded when the muscle relaxed. At least 20 supramaximal stimulations were applied in a random fashion, and mean F latencies were recorded from each of the extremities.

For measurement of the SSR, the same ENMG equipment was used. The skin temperature was maintained at 32°. Active surface electrodes were attached on the palmar side, and the references were placed on the dorsum of the hand. The stimulus was given at the wrist contralateral to the recording side. Measurements were taken from both arms. An intensity of 20-30 mA with an irregular interval of more than one minute was preferred to prevent habituation. When habituation occurred, stimulation was delayed for about three or four minutes. Skin potentials were recorded for a 10 second analysis period. The latency and peak to peak amplitude were determined. Mean values were used for each parameter. Sweep speed was 500 ms/div. Sympathetic skin response was considered absent if there was no response after 10 stimuli.

Informed consent was obtained before the examination and the local Ethical Committee of Kocatepe University granted approval for the study.

Statistical analysis

All parametric results were expressed as mean \pm SD for each group. For the analysis of gender in a matched case control, Mantel-Haenszel odds ratio was used. Statistical analyses were performed using the student t-test to compare mean values of F wave distal latency and the amplitude and distal latency of SSR between the groups. Results were reported in 95% confidence intervals. The correlation between the clinical findings

and electrodiagnostic tests was analyzed using the Spearman correlation. All analysis were performed using the SPSS (SPSS Inc., Chicago, Illinois, USA) 10.0 version for Windows software program.

RESULTS

All patients completed the study. No statistically significant difference was found in gender between the groups (odds ratio=1.27). Thirty-three patients in the FMS group and 27 patients in the control group were married. The clinical evaluation of the FMS patients and control group is shown in table 1.

The results of the blood count and routine biochemical parameters were within normal ranges for both groups.

In the evaluation of SSR, in FMS patients we observed a statistically significant decrease in distal latency, and a statistically significant increase in amplitude, when compared with the control group ($p<0.05$). However, no statistically significant difference was found in the distal latency of the F wave between the groups ($p>0.05$). The results are shown in table 2.

There was no statistically significant correlation between the SSR amplitude and distal latency results and VAS, BDS, FIQ and NTP scores in the FMS group ($p>0.05$). Also, no significant relationship was observed between F latency and clinical findings ($p>0.05$; Table 3).

DISCUSSION

The main symptom of FMS is diffuse, chronic pain. Upon clinical examination, no obvious systemic illness is diagnosed. In addition, clinical neurological examination and electrodiagnostic tests including needle ENMG and nerve conduction velocities are normal in FMS.^[14,15]

Table 1. Demographic data and clinical evaluation of groups

	Fibromyalgia syndrome (n=38)		Control (n=30)		p
	n	Mean \pm SD	n	Mean \pm SD	
Age (years)		40.6 \pm 9.6		39.5 \pm 9.0	0.707
Gender					
Female	37		29		0.330
Male	1		1		0.330
Disease duration (months)	12				
Visual analog scale	7				
Beck depression inventory	15				
Fibromyalgia impact questionnaire	63				
Number of tender points	14				

SD: Standard deviation.

Table 2. Electroneuromyographic evaluation of sympathetic skin response and F wave of fibromyalgia syndrome patients and controls

	Fibromyalgia syndrome (n=38)	Control (n=30)	95% Confidence interval	<i>p</i>
	Mean±SD	Mean±SD		
Right median SSR latency (sec)	1.3±0.3	1.5±0.2	0.36-0.08*	0.002
Left median SSR latency (sec)	1.3±0.4	1.6±0.2	0.46-0.18*	0.000
Right median SSR amplitude (mV)	3.4±1.9	2.2±1.4	0.37-2.0*	0.005
Left median SSR amplitude (mV)	3.2±1.8	2.3±1.5	0.13-1.7*	0.023
Right median F wave latency (ms)	27.2±2.1	27.6±2.6	-1.5-0.7	0.909
Right ulnar F wave latency (ms)	26.5±2.2	25.5±4.7	-0.7-2.7	0.806
Left median F wave latency (ms)	26.6±2.2	27.1±2.7	-1.6-0.6	0.751
Left ulnar F wave latency (ms)	26.6±1.9	26.5±2.3	-0.7-1.2	0.830

SD: Standard deviation; *: Statistically significant level; SSR: Sympathetic skin response.

Previous studies have investigated the role of autonomic nervous system dysfunction in FMS. The SSR which facilitates examination of the function of the autonomic nervous system simply, practically and effectively has been used extensively. Since the afferent and efferent pathways of the SSR are well known, it has been used in the clinical diagnosis of peripheral autonomic dysfunction for some cases.^[16-18]

Most of these previously mentioned studies have shown that increased sympathetic nervous system activity, or enhanced responsiveness to sympathetic activity, enhances symptoms in patients with FMS. Some of these studies showed elevated function in the sympathetic nervous system.^[4-7] Martinez-Lavin et al.^[19] suggested that fibromyalgia patients have norepinephrine-evoked pain which may be resolved by sympatholytic maneuvers. They also proposed that sympathetic hyperactivity may explain some of the manifestations of FMS including sleep disorders, irritable bowel syndrome, sicca symptoms and anxiety.^[20] Considering a hypothesis of alteration of muscle and tissue blood flow as well as participation of

the sympathetic nervous system, Bennett et al.^[21] have demonstrated excess Raynaud's-like symptoms and objective evidence of cold sensitivity in fibromyalgia. Twelve of 29 FMS patients had a decrease in finger systolic pressure of more than 20% after cooling. Additionally, Bengtsson and Bengtsson^[22] have noted that regional sympathetic blocks improved the symptoms.

In our study, fibromyalgia patients had significantly higher amplitudes and lower latencies for both sides when compared with controls. In other words, increased SSR amplitude and decreased SSR latency support the hypothesis of sympathetic nervous system alteration in our FMS patients. Many studies have shown increased amplitude and decreased latency in hemiplegic patients and in reflex sympathetic dystrophy patients as a sign of sympathetic overactivity.^[23,24] There are contradictory results regarding SSR latencies. Some studies have reported the intra-individual variations for amplitudes (2-48%) and latencies (2-22%).^[25,27-30] Although Özgöçmen et al.^[25] found a close correlation between SSR latencies

Table 3. Results of the correlation of electrodiagnosing tests and clinical evaluation in fibromyalgia syndrome patients group

	Fibromyalgia syndrome (n=38)		
	SSR (latency)	SSR (amplitude)	F wave latency
Visual analog scale	r=0.182 p=0.202	p=0.288 r=0.058	r=0.218 p=0.738
Beck depression inventory	r=0.053 p=0.690	p=0.757 r=0.308	r=0.069 p=0.067
Fibromyalgia impact questionnaire	r=0.192 p=0.778	p=0.261 r=0.106	r=0.049 p=0.540
Number of tender points	r=0.122 p=0.322	p=0.478 r=0.058	r=0.176 p=0.738

SSR: Sympathetic skin response; FMS: Fibromyalgia syndrome.

in hands and clinical parameters, they observed no statistically significant difference in SSR distal latency between FMS patients and controls. In another study, Ulaş et al.^[26] investigated the autonomic nervous system dysfunction in FMS patients. They found significantly longer SSR distal latencies which are in contrast with our results. Recently Eisinger^[31] reported that “fibromyalgia could be a generalized sympathetic dystrophy”. There is an ANS dysfunction in FMS; however, this may not present in the same way for all patients. Some studies support diminished sympathetic activity whereas others found increased activity. These results suggest that there is no accepted point of view, but this does not change the presence of alterations in ANS which our results support.

The F-wave has proven advantages for the evaluation of the conductivity and neuron activity in proximal portions of the motor nerves since the waves occur after impulses have traveled the entire length of the motor nerves. Both F wave conduction velocity and F wave occurrence rate reflect the function of motor nerve conductivity and motor neuron activity and have been used recently in the evaluation of peripheral nerve disorders.^[32,33] Previously, Ersoz^[10] evaluated nerve conduction tests in FMS patients and found no differences in F wave values performed from median, ulnar, tibial and peroneal nerves. In our study, no significant difference was found in the distal latency of the F wave between the patients and controls.

In conclusion, we can state that increased sympathetic nervous system activation occurs in FMS patients. We suggest that this abnormality could be successfully determined by SSR analysis which can be a useful and noninvasive method.

Declaration of conflicting interests

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