

Peak Oxygen Uptake and Ventilatory Anaerobic Threshold in Fibromyalgia

VALÉRIA VALIM, LEDA M. OLIVEIRA, ALINA L. SUDA, LUCIANA E. SILVA, MÁRIO FARO, TURÍBIO L. BARROS NETO, DANIEL FELDMAN, and JAMIL NATOUR

ABSTRACT. Objective. To compare maximum oxygen uptake and anaerobic threshold in patients with fibromyalgia (FM) and healthy sedentary controls matched by sex, age, weight, and body mass index.

Methods. Fifty women with FM aged 18–60 years and 50 healthy sedentary controls were studied. All were submitted to a maximum treadmill incremental test. Expired gas, ventilatory anaerobic threshold, and maximum oxygen uptake (VO_{2max}) were evaluated. The influence of FM on quality of life was evaluated by questionnaires: the Fibromyalgia Impact Questionnaire and the Medical Outcomes Study Short-Form (SF-36).

Results. In patients with FM, the anaerobic threshold and peak oxygen uptake were significantly reduced. Maximum heartbeat rate was significantly lower in FM, indicating submaximum effort. Linear regression data showed a correlation between peak VO_2 and the “Role-physical” domain of the SF-36. No such correlations were noted with anaerobic threshold.

Conclusion. These results confirm the hypothesis of lower physical fitness in patients with FM. Considering that patients with FM do not achieve a maximum effort, ventilatory anaerobic threshold should be considered as a better fitness index than VO_{2max} . (J Rheumatol 2002;29:353–7)

Key Indexing Terms:

FIBROMYALGIA FITNESS MAXIMUM OXYGEN UPTAKE ANAEROBIC THRESHOLD

Fibromyalgia (FM) is a chronic painful noninflammatory condition characterized by diffuse pain and multiple areas tender to palpation. Most patients show sleep disturbances and fatigue, which contribute to increasing disability^{1,2}.

Central changes in pain modulations with increased peripheral nociception are reported to be relevant in the development of symptoms in FM^{3–9}.

Several studies show nonspecific changes in muscle fibers in patients with FM, consistent with tissue ischemia attributed to physical inactivity^{10–18}. These peripheral changes, although unspecific, might be a factor involved in fatigue and pain amplification.

Despite widespread acceptance, the hypothesis that patients with FM are “more sedentary” than normal sedentary people is based on one study, showing that 80% of patients were considered below normal levels for maximum oxygen

uptake (VO_{2max}), according to the American Heart Association (AHA) standards¹⁸.

VO_{2max} is extensively used as a measure of cardiorespiratory physical fitness. It is the largest oxygen volume uptake by time unit on breathing atmospheric air during effort, and it is proportional to the product of heart output by the oxygen arteriovenous difference. Ventilatory anaerobic threshold oxygen uptake (VO_{2AT}), although used less than VO_{2max} , is also a good physical fitness indicator, and it has the advantage of not being maximum effort dependent, i.e., it does not depend on the individual’s will to cooperate¹⁹. The anaerobic threshold can be defined as the largest oxygen uptake reached without sustained lactacidosis²⁰. It can be measured either directly by lacticemia dosage or indirectly by analysis of expired gases. In this case it is called ventilatory anaerobic threshold. It seems to be more influenced by training than VO_{2max} and represents a safer intensity for exercise, thus decreasing the risk of lesions and constituting an important measure for prescription of exercise. The anaerobic threshold corresponds to roughly 60% of VO_{2max} in sedentary individuals and 73% in trained individuals²¹.

We undertook this study because of the scarcity of data on well controlled trials of physical fitness in FM and the absence of an established measure for physical fitness in FM.

MATERIALS AND METHODS

We studied 50 patients with FM (American College of Rheumatology 1990 criteria) aged between 18 and 60 years. Inclusion was based on the patient’s willingness to participate. Patients had to be free of any cardiorespiratory, articular, or neurologic disease that could limit a physical activity or ergometric test. All patients were women and were currently being seen at the outpatient clinic in the Federal University of São Paulo. All patients had a diag-

From the Rheumatology Division, Department of Medicine and Sports and Physical Medical Center, São Paulo Federal University, São Paulo, Brazil.

Supported by FAPESP (Research Support Fund of the State of São Paulo).

V. Valim, MD, Division of Rheumatology; L.M. Oliveira, Physiotherapist; A.L. Suda, Physiotherapist; L.E. Silva, Physiotherapist, Rheumatology Rehabilitation Section, Division of Rheumatology; M.Faro, MD, Sports and Physical Medical Center; T.L. Barros Neto, PhD, Head, Sports and Physical Medical Center; D. Feldman, MD, Professor, Division of Rheumatology; J. Natour, MD, Head, Rheumatology Rehabilitation Section, Division of Rheumatology.

Address reprint requests to Dr. J. Natour, Rheumatology Division, Universidade Federal de São Paulo, Rua Botucatu 740, 04023-900 São Paulo, Brazil. E-mail: jnatour@reumato.epm.br

Submitted January 23, 2001; revision accepted August 8, 2001.

nosis at the time of inclusion, without any previous treatment. Patients taking analgesics were required to discontinue them 15 days before the test.

Controls were enlisted after a computerized search of healthy sedentary individuals matched for sex, age, weight, and body mass index (BMI) who had performed the same tests before initiating any physical activity. We defined as sedentary that individual who did not take any method of physical exercise in the most recent 12 weeks. This information was received as an answer to a direct question.

All individuals submitted to a 13 min maximum spiroergometric test using a treadmill incremental test protocol, starting with a 3 min warmup period, on a 3 km/h load, with a 1 km/h increase every minute up to 7 km/h, and after that, a 2.5% slope inclination increase up to 15%²². The protocol was adequate for all the patients, i.e., none needed larger loads than those defined in the protocol to reach either the threshold or the maximum effort. The test was interrupted at the patient's request because of dyspnea, pain, or muscle fatigue. Heartbeat was recorded at the end of each stage.

Expired gas analysis was performed with a computerized metabolic system — Vista Mini-CPX (Vacumed, Ventura, CA, USA). From this analysis of the oxygen uptake the following variables were evaluated: ventilation per minute (VE), carbonic gas output (VCO₂), the ventilatory equivalent of oxygen (VE/VO₂) and carbonic gas (VE/VCO₂), and the respiratory quotient (RQ).

The highest value obtained in the last load was taken as peak oxygen uptake (VO_{2peak}). Anaerobic threshold was obtained from the average of the 3 values recorded for the load immediately before that in which the threshold occurred. The anaerobic threshold was defined by using the following criteria: nonlinear VE elevation, VE/VO₂, VE/VCO₂, and RQ curves' inflection point.

The percentage of oxygen utilization at the anaerobic threshold (%AT) in relation to maximum uptake ($\%AT = VO_{2AT}/VO_{2max} \times 100$) was calculated because it is a measure directly proportional to physical fitness²³. Heartbeat at the end of each stage and heartbeat maximum were monitored and recorded.

The influence of FM over quality of life was evaluated through a specific questionnaire, the Fibromyalgia Impact Questionnaire (FIQ)^{24,25} and a generic questionnaire, the Medical Outcomes Study Short-Form (SF-36)^{24,26,27}, administrated by a single interviewer. The SF-36 has 8 scales: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health²⁸. The FIQ is made up of 10 items, from which the total score is calculated. Pain was measured through the "pain" domain of SF-36 and FIQ-14.

Cardiorespiratory fitness levels were compared to those in the American Heart Association VO_{2max} table and VO_{2max} and VO_{2AT} tables of the Center for Physical and Sports Medicine (CEMAFE), obtained from normal sedentary Brazilian individuals²¹.

All the patients read and signed the consent terms. The institution's Ethics Committee approved the study.

Statistics. To compare the groups we used Student's t test for independent variables. Data were tested for normal distribution (Kolmogorov-Smirnov nonparametric test) and to check if variances were equal (Levene's nonparametric test). In all tests, the significance level was $\alpha = 0.05$. For those variables presenting non-normal distributions we used the Mann-Whitney test.

The correlation of quality of life and VO_{2max} and VO_{2AT} was evaluated through multiple linear regression analysis. The software used was SPSS, release 8.0.

RESULTS

Both groups were adequately matched for age, weight, and BMI values. There was a significant difference between the control and FM groups related to all spiroergometric variables. The VO_{2max} and VO_{2AT} were lower in the FM group compared to controls. Maximum and threshold heartbeat rates were higher in the control group. The percentage of oxygen utilization at the anaerobic threshold in relation to maximum uptake (%AT) was higher in the FM group (Table 1).

Table 1. Demographic and spiroergometric data, means ± standard deviation.

	Control (n = 50)	Fibromyalgia (n = 50)	p
Age, yrs	41.35 ± 8.49	41.2 ± 9.43	0.93
Weight, kg	65.4 ± 10.81	64.10 ± 12.90	0.58
BMI, kg/m ²	25.3 ± 4.43	25.81 ± 4.98	0.58
VO _{2max} , ml/kg/min	30.77 ± 5.56	25.64 ± 5.21	0.000001
VO _{2AT} , ml/kg/min	18.74 ± 3.86	16.35 ± 2.94	0.001
HR _{max} , bpm	174.07 ± 13.22	168.48 ± 13.67	0.04
HR _{AT} , bpm	140.14 ± 14.83	133.20 ± 14.63	0.01
%AT	61.22 ± 7.75	64.98 ± 10.8	0.04

VO_{2max}: maximum oxygen uptake (ml/kg/min), VO_{2AT}: anaerobic threshold oxygen (ml/kg/min), HR_{max}: maximum heartbeat rate (bpm), HR_{AT}: anaerobic threshold heartbeat (bpm), %AT: VO_{2AT}/VO_{2max}, BMI: body mass index.

Eleven patients and 25 controls reached the maximum estimated heartbeat rate for their age. In other words, only 22% of the patients with FM reached maximum test value. All patients in both groups reached the anaerobic threshold load. At the end of the test, heartbeat rate was elevated close to 97% of the estimated value in the controls and 75% in the patients with FM. This difference was significant ($p < 0.001$).

Linear regression analysis showed that, among the quality of life variables studied, only the role-physical scale of the SF-36 correlated to the maximum oxygen uptake (Figure 1). No scale of either SF-36 or FIQ correlated with the VO_{2AT}.

According to the AHA values, 46% of the patients with FM were below the mean levels for physical fitness. In the Brazilian population normality table for maximum oxygen uptake and anaerobic threshold, more than 80% were below the mean level (Table 2).

Patients with physical fitness below average (weak and very weak) presented worse results in both FIQ scores and the SF-36 role-physical scale than those with excellent, good, or fair fitness level (Table 3). There was no statistically significant difference for the other SF-36 scales. Using Brazilian normality criteria there was no difference for VO_{2max} and VO_{2AT} among groups with fitness levels either above or below average.

DISCUSSION

Several authors consider physical fitness a factor involved in FM pathogenesis²⁹⁻³¹. There is evidence that physical activity can modulate pain in FM. Sleep deprivation leads to myalgia among normal individuals, but not among athletes²⁹; exercise programs have beneficial therapeutic effects³¹ and regular physical activity was related to less intensity of symptoms³². Although Bennett, *et al* found that 80% of patients with FM present low aerobic fitness¹⁸, they did not observe any difference for VO_{2LA}, probably because they used a matched control population for that of VO_{2max}. Sietsema, *et al* found no difference between FM and sedentary control individuals

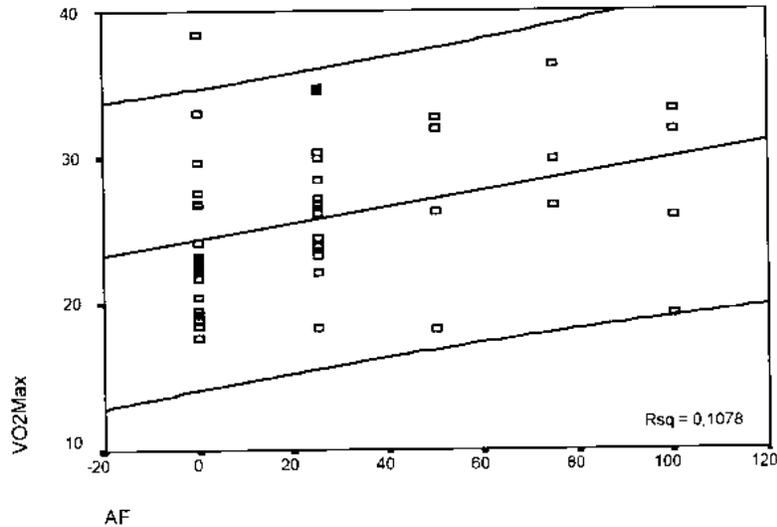


Figure 1. Correlation between SF-36 physical aspects domain (AF) and maximum oxygen uptake (VO_{2max}). $VO_{2max} = 24.243 + 0.05764 \times AF$; correlation, $r = 0.341$.

using VO_{2peak} and VO_{2LA} ³³. They included men in their sample. Even though this was a controlled study, the sample was very small.

Our study verified a statistically significant difference between FM individuals and sedentary controls in both maximum oxygen uptake and anaerobic threshold averages. This confirms and quantifies the low cardiorespiratory fitness level in patients with FM in relation to normal sedentary individuals.

Heartbeat is not a good physical fitness measure because it is very variable among individuals. However, the maximum

Table 2. Rate distribution of FM patients' aerobic fitness according to the American Heart Association (AHA) and Sports and Physical Medical Center–CEMAFE (Brazilian normal standards).

Classification	VO_{2max} AHA, %	VO_{2max} CEMAFE, %	VO_{2AT} CEMAFE, %
Very weak	10	58	50
Weak	36	28	28
Regular	44	6	12
Good	10	4	8
Excellent	0	4	2

Table 3. Comparison of SF-36 physical aspects domain and Fibromyalgia Impact Questionnaire (FIQ) scores between FM patients with above and below regular aerobic fitness level using American Heart Association criteria.

	Role Physical, SF-36	Total FIQ
Up (n = 27)	33.92 ± 32.78	4.45 ± 1.34
Below (n = 23)	12.5 ± 25.0	5.37 ± 1.33
p	0.006	0.02

SF-36: Short Form Health Survey.

heartbeat rate is a good indicator of maximum effort. In our study, only 22% of patients performed at maximum effort. Therefore, the oxygen uptake value reached at the end of the examination must be considered as VO_{2peak} and not as VO_{2max} . All the patients in both groups reached the anaerobic threshold load. Thus the anaerobic threshold is a more reliable index than the maximum uptake in patients with FM. The heartbeat at threshold or at any load immediately below this threshold indicates a training intensity adequate to gain cardiorespiratory fitness, with a lower risk of lesions and with higher adherence.

It is not clear if this VO_{2peak} and VO_{2AT} decrease happens as a consequence of reduction of daily physical activity caused by fatigue and pain³⁴. Probably the muscle metabolism is not primarily altered. Women with FM show worse physical performance³⁵ and functional limitation in daily physical activities²⁴, and many of them complain about pain worsening some days after exercises³⁶, thus feeding the pain/low fitness cycle.

Our study revealed a weak correlation between VO_{2max} and SF-36 (role-physical). This scale in the SF-36 questionnaire evaluates problems with work or other daily activities as a result of physical health. This suggests that individuals with more difficulties performing physical activities are those unable to reach a maximum test condition. We found no correlation between anaerobic threshold and role-physical or any other scale of SF-36 or FIQ. The weak correlation found between SF-36 “role-physical” and the VO_{2peak} , but not the VO_{2AT} , allows us to conclude that FM is a more complex syndrome than simple metabolic or sensorial disorders, showing an important compromise of behavioral and cognitive functions.

Our study does not show any relationship between aerobic physical capacity and pain level evaluated by the bodily pain scale of both SF-36 and pain FIQ. This result agrees with the

evidence that pain intensity is not related to physical limitation and dysfunction.

On grouping the patients with physical fitness levels below average levels, using maximum oxygen uptake criteria, we observed that these individuals presented worse scores for total FIQ and the role-physical scale of the SF-36, compared to individuals classified as above the average levels. We should take into consideration that correlating variables by group is only a rough way to observe a tendency, therefore these results must be carefully examined. Neither could we observe any difference in the instruments for quality of life among individuals either above or below average levels, using anaerobic threshold uptake criteria. This reinforces the impression that a worse effect on quality of life is not related to the cardiorespiratory fitness level.

Threshold heartbeat was lower in the FM group. This might be explained by an impaired regulation of the autonomic nervous system^{37,38}. We did not apply concomitant tilt test studies in the patients, thus it was impossible to verify this hypothesis.

The %AT is directly proportional to aerobic fitness. So the more fit the patient is, the closer to the VO_{2max} his/her VO_{2AT} should be. Paradoxically, the %AT was higher in patients with FM. This result could be due to underestimated VO_{2max} values consequent to submaximal effort test.

In accord with AHA criteria, 46% of patients with FM were below the average levels for cardiorespiratory aptitude. This percentage was higher (86%) using the Brazilian reference values, both for maximum uptake and for anaerobic threshold uptake. This difference can be explained by the population differences for weight, cultural habits, and physical activity level between the 2 populations. Thus we assume the more reliable result is obtained using the Brazilian reference values, which are in agreement with the world literature¹⁸.

In summary, our results confirm the hypothesis of lower physical fitness in patients with FM. Considering that patients with FM do not usually achieve a maximum effort, the anaerobic threshold should take into consideration a better fitness index than VO_{2max} . The classification of physical fitness might be useful for better understanding of FM subgroups, leading to better treatment protocols.

REFERENCES

1. Moldofsky H. Sleep and fibrositis syndrome. *Rheum Dis Clin North Am* 1989;15:91-103.
2. Wolfe F, Smythe HA, Yunus MB, et al. The American College of Rheumatology 1990 criteria for classification of fibromyalgia: report of the Multicenter Criteria Committee. *Arthritis Rheum* 1990; 33:160-72.
3. Russell IJ. Neurohormonal aspects of fibromyalgia syndrome. *Rheum Dis Clin North Am* 1989;15:149-68.
4. Russell IJ, Michalek JE, Vipraio GA, Fletcher EM, Wall K. Serum amino acids in fibrositis/fibromyalgia syndrome. *J Rheumatol* 1989;16 Suppl 19:158-63.
5. Russell IJ, Vaeroy H, Javors M, Nyber F. Cerebrospinal fluid biogenic amine metabolites in fibromyalgia/fibrositis syndrome and rheumatoid arthritis. *Arthritis Rheum* 1992;35:550-6.
6. Russell IJ, Michalek JE, Vipraio GA, Fletcher EM, Javors MA, Bowden CA. Platelet ³H-imipramine uptake receptor density and serum serotonin levels in patients with fibromyalgia/fibrositis syndrome. *J Rheumatol* 1992;19:104-9.
7. Russell IJ, Orr MD, Littman B, et al. Elevated cerebrospinal fluid biogenic amine metabolites in fibromyalgia/fibrositis syndrome and rheumatoid arthritis. *Arthritis Rheum* 1994;37:1593-601.
8. Vaeroy H, Helle R, Forre O, Kass E, Terenius L. Elevated CSF levels of substance P and high incidence of Raynaud phenomenon in patients with fibromyalgia: new features for diagnosis. *Pain* 1988;32:21-6.
9. Yunus MB, Dailey JW, Aldag JC, Masi AT, Jobe PC. Plasma tryptophan and other amino acids in primary fibromyalgia: a controlled study. *J Rheumatol* 1992;19:90-4.
10. Brendstrup P, Jespersen K, Ashoe-Hansen C. Morphological and chemical connective tissue changes in fibrositic muscles. *Ann Rheum Dis* 1940;2:114-26.
11. Awad EA. Interstitial myofibrositis. Hypothesis of the mechanism. *Arch Phys Rehabil* 1973;54:449-53.
12. Kalyan-Raman UP, Kalyan-Raman K, Yunus MB, Masi AT. Muscle pathology in primary fibromyalgia syndrome: a light microscopic, histochemical and ultrastructural study. *J Rheumatol* 1984;11:808-13.
13. Bengtsson A, Henriksson KG, Larsson J. Muscle biopsy in fibromyalgia. *Scand J Rheumatol* 1986;15:1-6.
14. Bengtsson A, Henriksson KG, Jorfeldt L, Kagedal B, Ennmarken C, Lindstrom F. Primary fibromyalgia: A clinical and laboratory study of 55 patients. *Scand J Rheumatol* 1986;15:340-7.
15. Bengtsson A, Henriksson KG, Larsson J. Reduced high-energy phosphate levels in the painful muscles of patients with primary fibromyalgia. *Arthritis Rheum* 1986;29:817-21.
16. Lund N, Bengtsson A, Thorborg P. Muscle tissue oxygen pressure in primary fibromyalgia. *Scand J Rheumatol* 1986;15:165-73.
17. Lindh MH, Johansson GA, Hedberg M, Grimby GL. Muscle fiber characteristics, capillaries and enzymes in patients with fibromyalgia and controls. *Scand J Rheumatol* 1995;24:34-7.
18. Bennett RM, Clark SR, Goldberg L, et al. Aerobic fitness in patients with fibromyalgia — a controlled study of respiratory gas exchange and ¹³³xenon clearance from exercising muscle. *Arthritis Rheum* 1989;32:454-60.
19. Koike A, Wasserman K, Taniguchi K, Hiroe M, Marumo F. The critical capillary PO₂ and the lactate threshold in patients with cardiovascular disease. *J Am Coll Cardiol* 1994;23:1644-50.
20. Wasserman K, Van Kessel AL, Burton GG. Interaction of physiological mechanisms during exercise. *J Appl Physiol* 1967;22:71-85.
21. Barros Neto TL, César MC, Tambeiro VL. Avaliação da aptidão física cardiorrespiratória. In: Barros Neto TL, Ghorayeb N. O exercício: preparação fisiológica, avaliação médica, aspectos especiais e preventivos. São Paulo: Editora Atheneu; 1999:15-24.
22. Fairshter RD, Walters J, Salness K, Fox M, Minh VD, Wilson AF. A comparison of incremental exercise tests during cycle and treadmill ergometry. *Med Sci Sports Exerc* 1983;15:549-54.
23. Hollmann W, Venrath H. Die Beeinflussung von Herzgrösse, maximaler O₂: Aufnahme und Ausdauergranze durch ein Ausdauertraining mittlerer und hoher Intensität. *Der Sportarzt* 1963;9:189-93.
24. Mannerkorpi K, Ekdahl C. Assessment of functional limitation and disability in patients with fibromyalgia. *Scand J Rheumatol* 1997;26:4-13.
25. Burckhardt CS, Clark SR, Bennett RM. Fibrositis Impact Questionnaire (FIQ): development and validation. *J Rheumatol* 1991;18:728-33.
26. Ciconelli RM, Ferraz MB, Santos W, et al. Brazilian Portuguese version of the SF-36. A reliable and valid quality of life outcome measure. *Rev Bras Reumatol* 1999;39:143-50.
27. Ware JE Jr, Sherbourne CD. The MOS 36-item Short-form Healthy

- Survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;30:473-81.
28. Ware JE Jr. SF-36 Health Survey update. *Spine* 2000;25:3130-8.
29. Moldofsky H, Scarisbrick P. Induction of neurasthenic musculoskeletal pain syndrome by selective sleep stage deprivation. *Psychosom Med* 1976;38:35-44.
30. Bennett RM. Physical fitness and muscle metabolism in the fibromyalgia syndrome: An overview. *Arthritis Rheum* 1989;32:454-60.
31. McCain GA, Bell DA, Mai FM, Halliday PD. A controlled study of the effects of a supervised cardiovascular fitness training program on the manifestations of primary fibromyalgia. *Arthritis Rheum* 1988;31:1135-41.
32. Granges G, Zilko P, Littlejohn GO. Fibromyalgia syndrome assessment of the severity of the condition 2 years after diagnosis. *J Rheumatol* 1994;21:523-9.
33. Sietsema KE, Cooper DM, Caro X, Leibling MR, Louie JS. Oxygen uptake during exercise in patients with primary fibromyalgia syndrome. *J Rheumatol* 1993;20:860-5.
34. Natvig B, Bruusgaard D, Eriksen W. Physical leisure activity level and physical fitness among women with fibromyalgia. *Scand J Rheumatol* 1998;27:337-41.
35. Mannerkorpi K, Burckhardt CS, Bjelle A. Physical performance characteristics of woman with fibromyalgia. *Arthritis Care Res* 1994;7:123-9.
36. Mengshoel AM, Vollestad NK, Forre O. Pain and fatigue induced by exercise in fibromyalgia patients and sedentary healthy subjects. *Clin Exp Rheumatol* 1995;13:477-82.
37. Claw D, Radulovic D, Antonetti D, Bagati R, Baraniuk J, Barberi JT. Tilt table testing in fibromyalgia [abstract]. *Arthritis Rheum* 1996;39 Suppl 9:S276.
38. Vaeroy H, Zhi-Gui Q, Morkrid L, Forre O. Altered sympathetic nervous system response in patients with fibromyalgia (fibrositis syndrome). *J Rheumatol* 1989;16:1460-5.