Vagal modulation and symptomatology following a 6-month aerobic exercise programme for women with Fibromyalgia

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ABSTRACT

Objective. *To examine the effects of a supervised aerobic exercise programme on heart rate variability (HRV) parameters and symptom severity in women with fibromyalgia (FM).*

Methods. *Thirty-two women with FM were randomly allocated to one of two groups: aerobic exercise (AE) or usual care control for 24 weeks. Women allocated to AE performed two aerobic exercise sessions per week of 45–60 min duration including 15–20 min of steady-state aerobic exercise at 60-65% of predicted maximum heart rate (HR_{max}) and 15 min of interval training at 75-80% HR_{max}, (six repetitions of 1.5 min, with 1 min interpolated rest intervals). Cardiac autonomic modulation was assessed using power spectral analysis of HRV. Symptoms severity was assessed by a 10 cm visual analogue scale (VAS) for pain, sleep disturbances, stiffness, anxiety and depression.*

Results. *After 24 weeks, the women in the exercise group showed an increase (4.8±0.2 to 5.2±0.2) in total power (LnTP, $p<0.001$), low frequency power (LnLF, $p<0.01$), high frequency power (LnHF, $p<0.001$), and the root-mean-square of successive R-R intervals (rMSSD, $p<0.001$). In addition, significant group-by-time interaction effects were observed for LnHF ($p=0.036$) and LnLF/HF ($p=0.014$). Improvements in anxiety and depression were also observed in AE versus control patients.*

Conclusio. *These results show that a programme of aerobic exercise training induced changes in cardiac autonomic nervous system modulation in FM and suggest that these changes in HRV parameters were accompanied by changes in anxiety and depression.*

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Introduction

Fibromyalgia (FM) is a syndrome of unknown origin characterised by chronic widespread musculoskeletal pain, fatigue, sleep disturbance, and joint stiffness (1). Although the aetiology of FM is not completely understood, there are multiple possible influencing factors, including genetic disposition and neural dysfunctions, resulting in amplification of pain transmission and interpretation (2). Using heart rate variability (HRV) analysis, studies have revealed reduced sympathetic nervous system reactivity and increased sympathovagal balance (3, 4), as well as reduced sympathetic reactivity under stress conditions in FM patients (5). It appears that many of the common FM symptoms (*e.g.* pain and fatigue) are attributed to autonomic dysfunction (6). In addition, improvements in the indices of HRV have led to clinical improvements in pain perception (7), suggesting that autonomic function could be relevant to FM symptoms.

A growing body of evidence supports the use of exercise training in the overall management of FM (8). Exercise training has demonstrated to be effective in improving symptoms, such as pain, sleep quality, stiffness, anxiety and depression (9-13). However, the potential role of exercise for modulating aspects of autonomic function in FM patients is largely unexplored. Only two previous studies have assessed the effect of exercise training on autonomic function in FM patients (7, 14). Kingsley *et al.* (14) showed that 12 weeks of resistance training reduces the severity of FM symptoms, but it had no impact on HRV. In contrast, Figueroa *et al.* (7) showed that a twice-weekly programme of resistance training for 16 weeks improved total power of HRV and parasympathetic activity in women with FM.

The importance of conducting further studies into the effects of exercise training on FM symptom relief and HRV parameters was recently highlighted by Kulshreshtha & Deepak (15). As the impact of aerobic exercise training on indices of cardiac autonomic function is

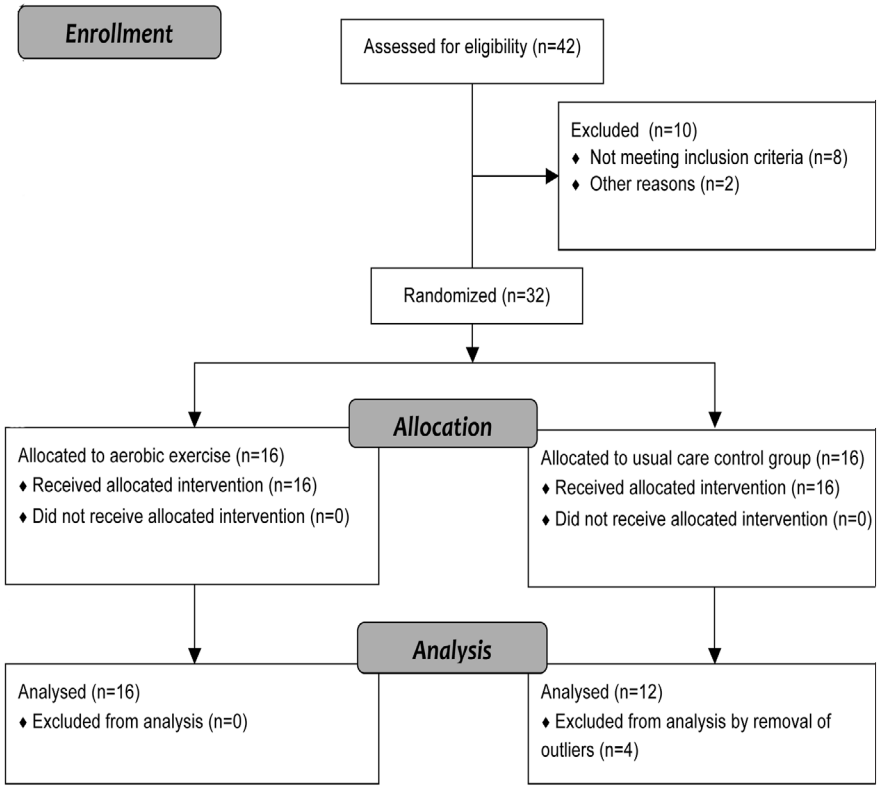

Fig. 1. Flowchart of the study.

unknown, the aim of this study was to assess the effects of an aerobic exercise programme on HRV parameters and symptom severity in women with FM.

Methods

Participants

Women with FM were recruited from local FM support groups in Spain according to the American College of Rheumatology guidelines (16) (Fig. 1). Participants were randomly assigned to an aerobic exercise group or a non-exercising control group for 24 weeks. Randomisation was undertaken by a member of the research team not directly involved in the recruitment or assessment of patients and was maintained blinded to the laboratory personnel involved in data collection.

Participants were excluded if they had pulmonary, cardiovascular, severe psychiatric or inflammatory rheumatic diseases. In addition, those who attended to psychological or physical therapy, or received exercise training in the last year, were excluded to avoid possible interactions with the present trial. All participants provided informed consent conformed to the declaration of Helsinki, which was approved by the University of Seville Research Ethics Committee.

Outcome measures

Participants were evaluated after fasting 10–12 h overnight and asked to refrain from caffeine intake and/or moderate to intense exercise at least 12 and 24 h before testing. Measurements at baseline and end of the study were collected at the same time of the day to reduce possible diurnal influences on HRV.

HRV data were collected following a 10 min period of supine rest using an Omegawave Sport Technology System (Eugene, OR). Among the most used HRV indices, the root-mean-square of successive R–R intervals (rMSSD) and high frequency (HF) power have been linked to vagal activity (17), while low frequency power (LF) is mediated by both sympathetic and parasympathetic activation. Total power (TP) of HRV is an estimation of the global activity of the autonomic nervous system and the LF/HF ratio is considered to reflect sympathovagal balance, usually interpreted as the relative sympathetic contribution to the control of heart rate (5).

All measurements were performed between 9:30 and 11:30 a.m. in a quiet temperature controlled room (23ºC). Participants were connected to electrocardiogram limb lead electrodes and data were recorded for 10 min. Spectral analyses of the R-R intervals were performed by fast Fourier transformation. The time domain index of HRV used in this study was the rMSSD. The total area under the curve was considered as the overall variability (TP). The power spectra were divided into the very low frequency band (0.004–0.40 Hz), LF band (0.04–0.15 Hz), and HF band (0.15–0.40 Hz). LF and HF were also converted to normalised units by expressing each power relative to the TP (nu= (LF or HF x 100)/ TP - very low frequency). The LF/HF ratio, considered to reflect sympathovagal balance, was also obtained. All analyses were conducted following the recommendation proposed in TaskForce (17).

Symptoms severity was measured by a 10 cm visual analogue scale for pain, sleep disturbances, stiffness, anxiety and depression. Participants rated each visual analogue scale from 0 representing an absence of the symptom to 10 indicating more severe symptomatology.

Exercise training programme

Women allocated to aerobic exercise group performed two sessions per week of 45–60 min duration. Each session included 10 min of warm-up activities (easy movements and slow walking), 15–20 min of steady-state exercise at 60–65% of predicted maximum heart rate (including continuous walking with arm movements and jogging) and 15 min of interval training at 75–80% (six repetitions of 1.5 min, with 1 min interpolated rest intervals), and 5–10 min of cool-down activities (slow walks, easy movements, relaxation training). Exercise intensity was monitored by a heart rate telemetric system (HOSAND® TM200, Hosand Technologies Srl, Italy). The intensity was progressively increased as participants improved their exercise capacity to maintain the heart rate in the prescribed range. During the 24-week intervention, participants in the control group continued their normal daily

activities, which did not include structured exercise.

Statistical analysis

Sample size was estimated using a mean difference of 387 for the primary outcome measure (TP) and a standard deviation of 170 (7), which gives a sample size of 8 per group. Allowing for an attrition rate of approximately 25% gives a total sample 20, providing 80% power at the 0.05 significance level. Data were tested for normal distribution (Kolmogorov-Smirnov non-parametric test) and all variables in absolute units were not normally distributed. Hence, HRV data were normalised using logarithmic-transformation (Ln) and outliers, which were >3 standard deviations from the sample mean, were removed from the analysis (n=4). Analyses were performed using SPSS 15.0 for windows (SPSS Inc, Chicago, IL, USA). Variables were analysed by a two-way analysis of variance with repeated measures (time: before and after 24 weeks; group: control and aerobic exercise group). When a significant time or group-by-time interaction was detected, within group comparisons were performed using paired t-tests.

Results

Table I shows the baseline characteristics of the two groups. The groups were well matched at the baseline assessment, with no apparent differences in key outcome variables.

Heart rate variability indices

Changes in HRV indices from baseline are presented in Table II. Analysis of the effect of exercise training on HRV revealed a significant effect of group in all variables. In the frequency domain, individuals in the aerobic exercise group had an increase in LnHF ($p<0.001$) and a decrease in LnLF/HF compared with the control group. Although there were significant increases in TP ($p<0.001$), LnLF ($p<0.01$), LnrMSSD ($p<0.001$) and HF (nu, $p<0.001$) together with significant decreases in LF (nu, $p<0.001$) and LF/HF (nu, $p<0.001$) in the aerobic exercise group, these changes were not significant compared with the control group.

Table I. Baseline values for the two groups.

Variable	Control (n=12)	AE (n=16)
Age (years)	58 ± 2	55 ± 2
Height (m)	1.57 ± 0.01	1.58 ± 0.01
BMI (kg/m^2)	29.7 ± 1.1	29.6 ± 1.1
Total power (ms^2)	189 ± 37	156 ± 35
LF (Hz)	90 ± 18	76 ± 22
HF (Hz)	43 ± 8	28 ± 5
LF/HF	2.2 ± 0.2	2.7 ± 0.4
rMSSD (ms)	13.2 ± 1.3	16.9 ± 2.3

Data are mean ± SE. AE: Aerobic exercise; rMSSD: root-mean-square of successive R-R; HF: high frequency power; LF: low frequency power (LF); LF/HF: sympathovagal balance.

Table II. Heart rate variability and symptoms severity before and after 24 weeks of control and endurance training.

	Control (n=12)		AE (n=16)	
Variable	Before	After	Before	After
LnTP	4.9 ± 0.2	5.2 ± 0.2	4.8 ± 0.2	5.2 ± 0.2‡
LnLF	4.1 ± 0.3	4.4 ± 0.3	3.9 ± 0.2	4.4 ± 0.3†
LnHF	3.4 ± 0.3	3.7 ± 0.3	3.1 ± 0.2	3.8 ± 0.2‡[a]
LnLF/HF	1.2 ± 0.1	1.2 ± 0.1	1.3 ± 0.1	1.1 ± 0.1‡[a]
LnrMSSD	2.5 ± 0.1	2.7 ± 0.1	2.7 ± 0.1	2.9 ± 0.1‡
LF nu	67.0 ± 6.7	66.4 ± 11.0	69.2 ± 12.8	59.8 ± 14.7‡
HF nu	33.0 ± 6.7	34.8 ± 10.7	30.8 ± 12.9	36.9 ± 14.8‡
LF/HF nu	2.2 ± 0.7	2.3 ± 1.6	2.7 ± 1.4	2.0 ± 1.0‡
Stiffness	6.4 ± 3.3	6.8 ± 2.2	5.3 ± 3.1	4.1 ± 2.3
Sleep disturbances	8.4 ± 2.2	8.6 ± 1.9	7.5 ± 3.2	7.2 ± 2.8
Pain	7.2 ± 1.8	7.0 ± 1.7	7.4 ± 2.2	6.7 ± 2.2
Anxiety	6.4 ± 3.0	7.5 ± 2.5	6.9 ± 3.3	5.7 ± 3.3*[a]
Depression	7.1 ± 2.7	6.7 ± 2.2	6.5 ± 3.7	5.6 ± 3.4*

Data are mean ± SE. AE: Aerobic exercise. TP: total power; LF: low-frequency; nu: normalised units; HF: high-frequency; Ln: natural logarithm; RMSSD: root mean square of successive differences of NN intervals.
*$p<0.05$, †$p<0.01$, ‡$p<0.001$ *vs*. before (paired *t*-test). [a]$p<0.05$ group x time interaction.

Symptoms

Symptom severity did not differ significantly between groups at baseline (Table II). Anxiety decreased (-17%; $p=0.02$) in the aerobic exercise group compared with the control group. However, the decrease in depression (-14%; $p<0.05$) observed in the aerobic exercise group was not different than the no change in the control group.

Discussion

The aim of this study was to evaluate the effect of a 6-month aerobic exercise programme on HRV parameters and symptom severity in women diagnosed with FM. The results of this study indicated that aerobic exercise training can improve HRV, primarily by increasing cardiovagal modulation. Significant improvements were also found in anxiety and depression in the exercising group.

Our results showed high sympathetic activity at rest, as previously reported in FM patients (4, 5, 18). However, there are very few studies on HRV indices before and after exercise training in women with FM. It has been suggested that long-term programmes (more than 8 weeks) of moderate–high intensity aerobic exercise are needed to enhance HRV (19, 20), as low intensity exercise programmes seem to have no impact on HRV in healthy middle-aged and older men (21). The results of this study are in agreement with other studies of older healthy adults, which showed an increase in indices of cardiac vagal tone in the time and frequency domain after programmes of moderate intensity aerobic exercise (19, 22). However, this has not been a consistent finding (23, 24) and inconsistencies could be attributable to differences in training load.

Patients in the aerobic exercise group showed evidence of changes in HRV, with a predominance of parasympathetic indices after the intervention, suggesting that the intensity, frequency and duration of exercise was effective for improving vagal modulation in women with FM. Absolute LF power increased in the aerobic exercise group (11%), while normalised LF (14%) and sympatho-vagal balance (LF/HF) (15%) decreased with aerobic exercise. Consistent with our findings, previous studies have shown an increase in absolute LF power concurrently with increases in parasympathetic activity and TP after aerobic exercise training in middle-aged overweight and obese adults (22, 25-27). However, this is the first study to report such changes in women with FM after a programme of aerobic exercise, in conjunction with improvements in FM symptoms (anxiety and depression). LF power reflects parasympathetic and sympathetic modulation or sympathetic activity when expressed in absolute and normalised units (proportion of the TP), respectively (17, 28). Hence, the decrease in normalised LF is indicative of a reduction in sympathetic activity (17) and it is likely that an increase in parasympathetic activity is responsible for the increase in absolute LF (and TP) after aerobic exercise training (22). As a consequence, our results show that sympathovagal balance was shifted to parasympathetic predominance in women with FM, indicating improved cardiac autonomic modulation after aerobic exercise training.

Improvements in anxiety and depression were observed in the aerobic exercise group, in accordance with previous exercise intervention studies in women with FM (10-13). However, the changes in pain, sleep disturbances and stiffness were not statistically significant. Some authors have reported reduced levels of pain after long-term exercise interventions in women with FM (11-13, 29) and although in the current study improvements were not significant, women with FM experienced a 9% decrement, which is in line with the 8% reported by Tomás-Carús *et al*. (12) following 8 months of supervised exercise therapy. The changes in perceived sleep disturbances (4% for aerobic exercise group) are also in agreement with those reported after 16 weeks of aerobic exercise (30). However evidence regarding the effect of exercise on sleep quality is less clear. The main non-significant benefit in symptom severity was found for stiffness (23%), a much greater effect than the 1-8% reported in other long-term exercise programmes (12, 13, 30). It is likely that the present study was insufficiently powered to detect statistically significant changes in pain, sleep disturbances and stiffness. Nonetheless, our findings show that aerobic exercise training could be added to rehabilitation programmes for the management of cardiac autonomic dysfunction in women with FM and the attenuation of anxiety.

The main limitation of the present study is the small sample size, which may have resulted in type 2 errors; hence, caution has to be taken concerning the generalisation of our results. Future studies should consist of an adequate number of subjects to detect true differences between groups. Another limitation concerns the number of patients excluded from analysis by removal of outliers (n=4). Based on the literature, there are confounding factors in the measurement, analysis and interpretation of HRV such as posture or breathing frequency and possible artifacts (such as ectopic beats or arrhythmic events) distorting the signal and leading to calculation errors. Thirdly, high rates of comorbid depression and anxiety disorders may also affect autonomic cardiovascular control in women with FM. It is possible that our HRV results may have been confounded by the impact of various medications and symptoms on the autonomic nervous system.

Conclusions

Our results suggest that women with FM gain health benefits and improved cardiac autonomic nervous system modulation by engaging in moderate-to high-intensity aerobic exercise training. Further studies, aimed at investigating HRV indices with different forms exercise training and associations with FM symptom severity, are clearly warranted.

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