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Effects of resistant exercise and aerobic exercise on people with fibromyalgia syndrome: a systematic review of randomized clinical trials

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ABSTRACT

Introduction: Fibromyalgia syndrome (FMS) is characterized as a condition of chronic and generalized muscle pain, resulting primarily in decreased functional capacity and emotional changes of the patient. Physical exercise (PE) can promote different effects in FMS depending on the chosen method: aerobic training (AT) alone, resistance training (RT) alone or the combination of both in concurrent training (CT). **Objective:** To synthesize data from clinical trials on the effects of resistance training and aerobic training in people with FMS. **Methods:** Searches were performed in the Pubmed, Scielo, Virtual Health Library, Scopus and Web of Science databases. Articles published between 2009 and 2020 were analyzed. **Results:** Eighteen randomized clinical trials were included to compose the discussion of this review. Altogether 1,136 individuals with FMS who participated in interventions with PE were analyzed; 10 studies used RT as an intervention method; 8 applied AT and 3 used CT. In 3 studies more than one method was used. Studies pointed out that there were significant improvements in biological and psychophysiological aspects at the end of the interventions. **Conclusion:** The analyzed articles suggested that PE through both RT and AT, alone or combined, is an alternative treatment for the population with FMS, being a low-cost intervention and providing significant improvements for these patients.

Keywords: fibromyalgia; pain; exercise; quality of life.

INTRODUCTION

Fibromyalgia syndrome (FMS) affects about 5% of the world population[1]. In Brazil, it is estimated that about 2.5% of the population is affected, with a higher prevalence in women between 34 and 44 years of age[2,3]. There is great difficulty in FMS diagnosis due to the subjectivity of some tests. Investigation of FMS should be systemic, considering several physiological and psychophysiological aspects, such as reduction of functional capacity, sleep disorders, fatigue, quality of life and symptoms of depression and anxiety, along with sensitivity to pain in at least 11 of 18 tender points[4].

The reduction in quality of life in FMS is correlated with the level of extent of patients' pain, also reflecting the emergence of possible emotional disorders, such as anxiety and depression disorders, which can lead to sleep disorders[2]. The treatment of the syndrome relies on interdisciplinary interventions with non-pharmacological and pharmacological strategies.

Physical exercise (PE) is a non-pharmacological treatment that works mainly by pain reduction and restoration of quality of life of patients with FMS[5], being very important for improvement or maintenance of muscle strength and avoiding loss of physical functionality, commonly reported symptoms[6]. In addition, PE contributes to the promotion of general physical well-being through reductions in pain indices and possible improvements in quality of life. Moreover, it also promotes benefits in emotional health, such as the reduction of depression rates[7].

Considering the heterogeneity of this syndrome, with very specific action for each individual, updated evidence is relevant to provide directions for a more accurate and explicit prescription of PE for this population, easing the life with FMS in the face of increased benefits of physical activity and minimization of possible side effects of the syndrome.

Therefore, this study based on data from the scientific literature aimed to analyze the effects of resistance training and aerobic training in people with fibromyalgia syndrome through a systematic review.

METHODS

Determination of databases, search strategy and combinations

The systematic review of the literature was based on bibliographic research of randomized clinical trials between 2009 and 2020 that analyzed the effects of physical exercise in patients with FMS. The articles were searched in the electronic databases PubMed, SciELO, Virtual Health Library (VHL), Scopus and Web of Science simultaneously by two independent researchers in May 2020.

In the clinical question based on evidence, the PICO strategy was used: P - Participants clinical trials on FMS; I - Clinical trials with resistance exercise or aerobic exercise; C - Comparations of the results with the respective control groups; O – Effects of physical training on biological and psychophysiological variables.

The selection of the descriptors used was made using MeSH (Medical Heading Subjects). The descriptors and terms "Fibromyalgia", "Resistance training", "Aerobic training", "Aerobic exercise", "Strength training", "Endurance training" and "Resistance training" were used in the following combinations "Fibromyalgia" AND "Aerobic exercise", "Fibromyalgia" AND "Resistance training", "Fibromyalgia" AND "Endurance training"," and "Strength training", "Fibromyalgia" AND "Aerobic training".

Stages of the search plan

The search plan was divided into four stages. In the first stage, 1,987 publications potentially eligible for the review were identified. In the second stage, the filters of the year "2010 to current" and "human" were used. The first filter is explained by the fact that the studies that brought a more elaborate and systematic consensus on the diagnosis are concentrated in this decade; the second "human" filter was used to converge in studies closer to the proposed theme, resulting in 334 studies.

In the third stage, the titles, abstracts and conclusions of the studies were read in order to verify the adequacy to the purpose of this review. In addition, the inclusion criteria established for the selection of articles were applied by the researchers. Studies were included: a) randomized clinical trials; b) evaluations of the effect of aerobic exercise, resistance exercise or concurrent exercise on people with FMS. After the analysis of the studies, 67 publications were selected, because they met the inclusion criteria and began to be analyzed in the next stage.

In the fourth stage of the selection of articles, the exclusion criteria established according to the proposed objective were applied. Initially, the articles were initially read in full by two independent researchers: a) studies that reached less than 10 points in the critical review form of Law et al.[7]; b) studies that analyzed metabolite parameters - lactate, myokines, glucose and others; c) aquatic aerobic exercises; d) articles that used other intervention methods besides physical exercises. At the end of the fourth stage, 19 publications remained for review, as shown in Figure 1.

All stages of search and analysis of the studies by the two independent researchers were analyzed in the statistical software SPSS 22.0, the Kappa agreement test[8], to verify the agreement between the examiners. In this analysis, values up to 0.19 indicate poor agreement, between 0.20-0.39 agreement, 0.40-0.59 moderate agreement, 0.60-0.79 substantive agreement and between 0.80-1.00 indicates almost perfect agreement. Observed values were always above 0.80, with $p<0.001$, indicating almost perfect agreement among the researchers[8]. For a better understanding of the results, Figure 1 presents the quantitative studies during all stages.

Table 1 shows the score obtained by the selected studies in the critical review form of Law et al.[7]. This instrument aims to classify the quality of the studies[9-26], originally having 15 questions. However, item 4 does not score, because it is only to distinguish the type of study. Thus, item 4 was removed from our analysis. Item 5 became 4 and so on, totaling 14 scoring questions.

A quality cutoff point of 10 points was defined. Any article that did not score at least 10 points would be eliminated from the review. The items that were scored were marked with an "x", and those that did not score were marked with a "-".

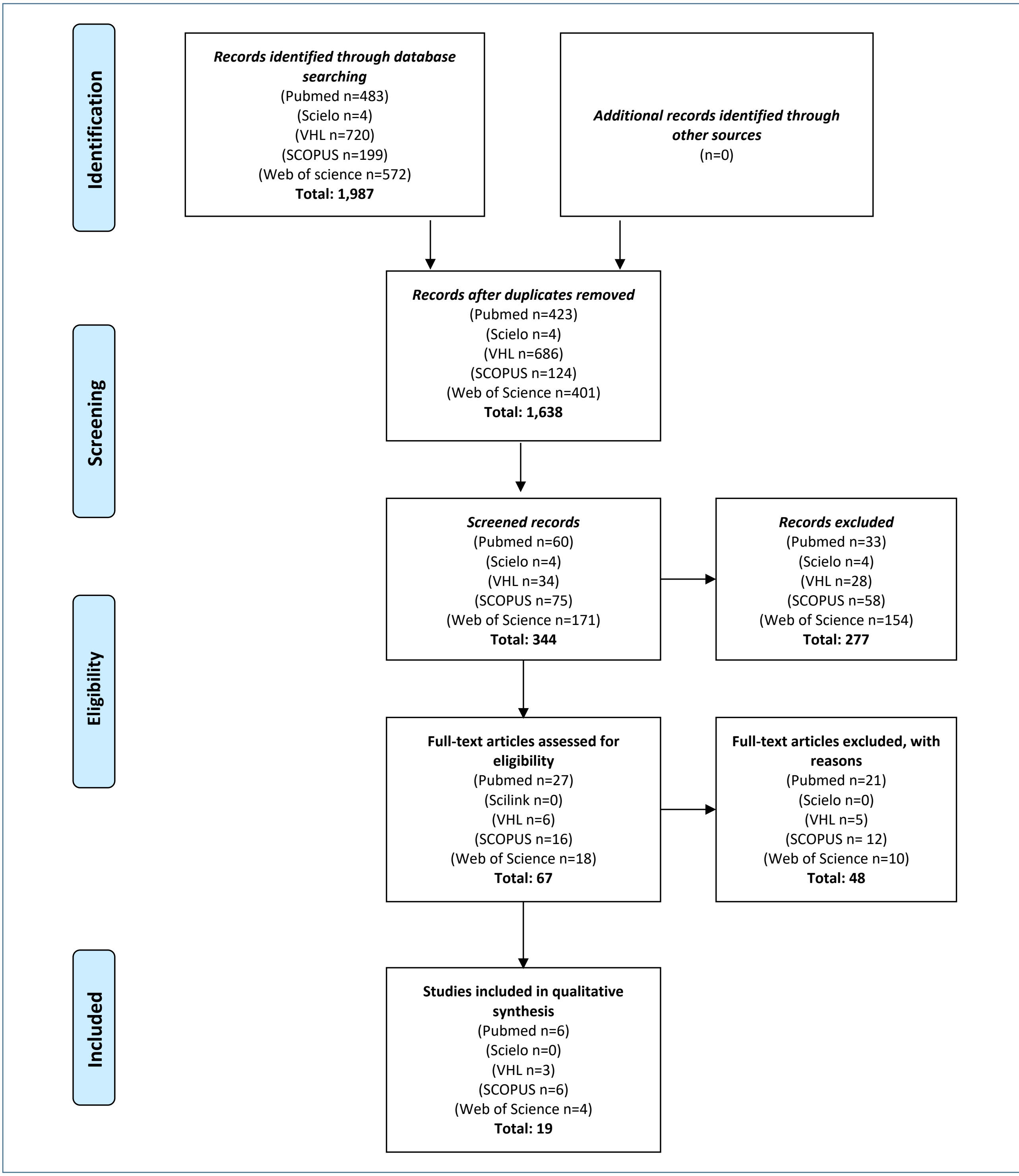

Figure 1: Flowchart of search steps.

RESULTS

Table 2 summarizes the profile of the selected studies. Approximately 45% of the articles compared resistance training (RT) with an active or non-active control group (CG). About 31% of studies compared the results of aerobic training (AT) *versus* the control group. Near 22% were about concurrent training (CT). The studies included a total of 1,136 patients, more than 90% of them women.

In Table 3, studies that used RT are listed. Fifty percent of the articles compared physical responses together with psychophysiological responses before and after the intervention. In addition, another 50% analyzed only psychophysiological responses, such

Table 1: Scoring the studies using the criteria of Law *et al*. [7].

Author/year	1- Clear purpose?	2- Literature revised?	3- Detailed sample?	4- Sample calculation	5- Confidence Measures	6- Validity measures	7- Intervention description	8- Contamination avoided?	9- Co-intervention avoided?	10- Report results	11- Statistical analysis	12- Clinical importance	13- Drop out	14- Conclusions	Total
Assumpção et al. 2018	X	X	X	X	X	X	X	X	X	X	X	X	-	X	13
Silva et al. 2019[10]	X	X	X	X	X	X	X	X	X	X	X	X	-	X	13
Kaleth et al. 2013[1]	X	X	X	X	X	X	X	X	X	X	X	X	-	X	13
Larsson et al. 2015[1]	X	X	X	X	X	X	X	X	X	X	X	X	-	X	13
Mannerkorpi et al. 2010[13]	X	X	X	X	X	X	X	X	X	X	X	X	-	X	13
Palstam et al. 2016[14]	X	X	X	X	X	X	X	X	X	X	X	X	-	X	13
Gavi et al. 2014[15]	X	X	X	X	X	X	-	X	X	X	X	X	-	X	12
Hooten et al. 2012[16]	X	X	X	X	X	X	X	X	-	X	X	X	-	X	12
Kayo et al. 2012[17]	X	X	X	X	X	X	X	-	X	X	X	X	-	X	12
Sañudo et al. 2015[18]	X	X	-	X	X	X	X	X	X	X	X	X	-	X	12
Wang et al. 2018[19]	X	X	X	X	X	X	-	X	X	-	X	X	-	X	11
Sañudo et al. 2010[20]	X	X	X	-	X	X	X	X	X	X	X	X	X	X	12
Sañudo et al. 2012[21]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	14
Medeiros et al. 2020[2]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	14
Ribeiro et al. 2018[2]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	13
Gómez-Hernández et al. 2020[24]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	13
Valmaña et al. 2020[25]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	13
Carbonell-Baeza et al. 2012[26]	X	X	X	X	X	X	X	X	X	X	X	X	-	X	13

X: adequate; -: inadequate

as pain threshold and depression. In addition, 50% of the articles analyzed whether or not there was an increase in strength after the intervention. A significant improvement in muscle strength was observed after the intervention.

In Table 4 it is possible to observe the results related to AT. All the included studies brought analyses of the physical responses linked to psychophysiological responses after the intervention. It can be observed that AT improved the peak VO2 of individuals.

In Table 5, which shows the studies that used AT as at least one of the intervention methodologies, 50% of the studies brought analyses of the physical responses tied to psychophysiological responses after the intervention. 16% of the articles analyzed the peak of VO2 of the individuals and showed that when compared to RT, the AT group presented an advantage in the variable analyzed.

In addition, Table 5 shows the studies related to CT. Thus, it can be perceived that this intervention improves variables related to physical function, psychophysiological responses and the general well-being of the individual.

DISCUSSION

This study aimed to systematically review clinical trials on the effects of RT and AT in people with FMS. The main findings of this review were that both resistance exercise and aerobic exercise are capable of promoting the reduction of pain perception and increased quality of life in these individuals. With regard to biological variables, specific gains were found for the type of training adopted. For example, strength gain for resistance training and increased aerobic fitness in aerobic training.

Despite the heterogeneity of the instruments used to measure the psychophysiological variables used by the studies, they are validated by the literature for this population[27,28]. With regard to biological variables, the tests used by the reviewed studies comply with the recommendations of the scientific literature[29].

In view of the need for analysis of psychophysiological issues, the studies used the application of questionnaires related to the quality of life of individuals affected with fibromyalgia and for the analysis of biological responses to training, specific tests were used that included body actions corresponding to physical fitness.

Resistance exercise and psychophysiological variables

RT has been an important tool to promote pain severity in people with FMS. This finding was already identified from three weeks in the study by Hooten et al.[16]. The RT was performed with moderate loads, where 10 maximum repetitions were reached. In another study with a longer duration, Larsson et al.[12], after 15 weeks, showed improvements in pain intensity in response to RT. The findings of both refer to the knowledge that the practice of

Table 2: Profile of selected studies.

Training	Study	Sample (n, gender and age)	Method of analysis
'Resistance Training	Assumpção et al. 2018	N=53 W; 30 to 55 years RG=19; SG=18; CG=16	FIQ, Clinical Improvement, SF-36
	Carbonell-Baeza et al. 2010[26]	N=75 W; 43-58 years old IG=33; CG=32	Conventional Borg Scale, Psychological Educational Therapy, BMI, %G
	Silva et al. 2019[10]	N=60 W; 18 to 60 years RT=30; CG=30	1RM, VAS.
	Larsson et al. 2015[12]	N=130 W; 22 to 64 years old RT=67; CG=63	1RM, FIQ, SF-36, PCS, MCS, VAS, 6MWT, PDI, CPAQ.
	Palstam et al. 2016[14]	N=130 W; 20 to 65 years RT=67; CG=63	Stepwise Multivariable Regression.
	Gavi et al. 2014[15]	N= 80 W; 18 to 65 years RT=35; FLEX=31	VAS, FIQ, IDATE, Hand Grip, VO2max., Dynamometry, HRV, SF-36
	Hooten et al. 2012[16]	N=72 (64W, 8H); Over 18 years; ATG=36; GTR=36	Analysis of VO2, Multidimensional Pain Inventory.
	Kayo et al. 2012[17]	N=90 W; 30 to 55 years; AT=30; RT=30; CG=30	VAS, SF-36, FIQ.
	Ribeiro et al. 2018[23]	N=32 W; 20 to 55 years	VAS, SF-MPQ.
	Medeiros et al. 2020	N=42 W; 18 and 60 years MPG=22	FIQ, SF-36, VAS, PSQI, PRCTS, FABQ
Aerobic Training	Gómez-Hernández et al. 2020[24]	N=64 W; 54.27±6.94 years old AT=32	PSQI, ESS, FIQ, VAS.
	Mannerkorpi et al. 2010[13]	N= 67 W; 48±7.8 years NW=28; LIW=26	FIQ, Exercise Heart Rate, 6MWT, MFI-20.
	Kaleth et al. 2013[11]	N=170 (9 M, 161 W); 18 to 65 years * SUS-PA=27; UNSUS-PA=68; LO-PA=75	CHAMPS, FIQ-PI, PHQ-8, BDI
	Hooten et al. 2012[16]	N=72 (64 W), (8 M); Over 18 years; AT=36; GT=36	Analysis of VO2, Multidimensional Pain and Strength Inventory.
	Kayo et al. 2012[17]	N=90 W; 30 to 55 years; ATG=30; GTR=30; CG=30	VAS, SF-36, FIQ.
	Sañudo et al. 2015[18]	N= 42 W; 53 to 60 years ATG=16	HRV, VAS, sleep disorders, stiffness, anxiety and depression.
	Valmaña et al. 2020	N=50 W; 40 to 75 years IG=23	VAS, FIQ, SF-36.
	Wang et al. 2018[19]	N=226 (208 W, 18 M); 52 years old ($\bar{X}$) ATG=75; **Tai Chi Groups G1=39; G2=37; G3=39; G4=37	FIQ, HADS, BDI, SF-36.
Concorrente Training	Sañudo et al. 2010	N=30 W; 59±7.9 years IG=15; CG=15	FIQ, Functional Capacity, SF-36
	Sañudo et al. 2012	N=41 W; GT=21	FIQ, SF-36, BDI, 6MWT.
	Valmaña et al. 2020	N=50 W; 40 to 75 years IG=23	VAS, FIQ, SF-36.

1RM: One-repetition maximum test; 6MWT: 6-minute walk test; ATG: Aerobic Training Group; BDI: Beck Depression Inventory; CG: Control Group; CHAMPS: Community Health Activities for the Elderly; CPAQ: Chronic Pain Acceptance Questionnaire; CT: Concurrent Training; PCS: Physical Component Scale; MCS: Mental Component Scale; EG: Experimental group; ESS: Epworth Sleepiness Scale; FABQ: Fear Avoidance Beliefs Questionnaire; FIQ: Fibromyalgia Impact Questionnaire; FLEZG: Flexibility Group; HADS: GT: training group; Hospital Anxiety and Depression Scale; HRV: Heart Rate Variability; IDATE: IDATE Trait-State; IG: Intervention Group; LIW: Low intensity walking; M: Men; MFI-20: Multidimensional fatigue inventory; N: Sample number; NW: Nordic Walking; PDI: Pain Disability Index; MPG: Mat Pilates Group; PHQ-8: Patient Health Questionnaire-8; PRCTS: Catastrophic Thoughts on Pain Scale; PSQI: Pittsburgh Sleep Quality Index; RG: Resistance Group: SF-36: Short Form 36 Health Survey Questionnaire; SF-MPQ: Short Form McGill Pain Questionnaire; SG: Stretching Group; VAS: Visual Analog Scale; W: Women.
* SUS-PA: MET h wk of increase in MVPA and sustained; UNSUS-PA: Increase ≥10 MET h/wk in MVPA, followed by decline; LO-PA: It did not reach a ≥10 MET h/wk in MVPA (LO-PA).
** Tai Chi Groups: G1 (1 session/week for 12 weeks); G2 (2 sessions/week for 12 weeks); G3 (1 session/week for 24 weeks); G4 (2 sessions/week for 24 weeks)

RT in the short/medium term can promote important decreases in the severity of pain of patients with FMS.

Pain is one of the most striking symptoms of FMS and is related to nociceptive hypersensitivity in the central nervous system, generating hyperalgesia. This effect leads to exaggerated perceptual responses in these patients[30]. Still explaining the physiological mechanism of pain, the study by Bjersing et al.[31], found an association with the metabolites Insulin-like growth factor (IGF-1) and leptin. After 15 weeks of RE, alterations of these metabolites were associated with reduced pain and fatigue, due to both metabolites

Table 3: Outcome from studies related to Biological and Psychophysiological Responses to Resistance Training

Author/ year	Variable analyzed	Exercise applied and Weekly frequency/duration	Exercise applied and Weekly frequency/ duration	Biological responses to physical training	Conclusions
Assumpção et al. 2018[9]	Pain threshold, sensitive points, Qol, vitality and mental health.	GTR:1 series of 8 rep's. for 8 full body exercises. SG: Stretching for the whole body. 2 sessions/week for 40 min. for 12 weeks.	^ QoL, vitality and mental health (measured by SF-36) compared to baseline. ↑* in FIQ physical functioning; * Improves fiq depression score. ↑* at pain threshold, number of tender points and impact on FMS symptoms.	Not observed in the study	Muscle stretching was the most effective modality in improving QoL, especially in physical functioning and pain. RT was the most effective modality in reducing depression.
Silva et al. 2019[10]	Pain significance and FM.	GTR:1 series of 8 rep's. for 8 whole/body exercises. GS: Exercises based on relaxation and sophrology for the whole body. 2 sessions/week for 40 min. for 12 weeks.	^ QoL, vitality and mental health (measured by SF-36) compared to baseline. ↑* in FIQ physical functioning; * Improves fiq depression score. ↑* on pain threshold, number of tender points and impact on FMS symptoms.	↑ in strength in the 7 muscles evaluated in the TR (as compared to baseline). ↑* in the 6-minute walk test and TCN in the TR. ↔* compared to 1RM for the GS group.	The GS presented intragroup ↑* for the TCN test and in the domains social aspects, general health status and pain of the SF-36. The TR was more effective in the FM ↑, in the performance in the 6MWT and in the functional capacity domain of the SF-36 compared to the GS.
Larsson et al. 2015[12]	FM, pain intensity, physical capacity, health status and health problems in chronic pain.	CG: 50 minutes, including exercise for the whole body + 10 minutes of stretching. GTR: 1 to 2 series of 15 – 20 rep's. to 40% of 1 RM ↑ gradual of 20% of 1RM over the weeks up to 80% of 1RM. 2 sessions/week for 15 weeks.	↑* in health-related QOL (SF-36, ECF and McE) in the Wg. •* in painful disability (IID) in the TG compared to the CG. •* in the current pain intensity (VAS) in the TG compared to the CG. ^ * in health status (total FIQ score) in the TG compared to the CG.	↑* for isometric knee extension strength in the TG compared to the CG. ↑* in the isometric force of elbow flexion in the TG compared to the CG. ↔ * between groups in handgrip strength; ↑* in both groups compared to the baseline in their strength.	Progressive RT proved to be a viable mode of exercise for women with FMS, improving muscle function, health status, current pain intensity, pain control and participation in activities of daily living.
Palstam et al. 2016[14]	Average incapacity for pain and physical capacity.	GTR: Start with 10 min. warm-up, training at 40% of 1RM; ↑ progressive up to 80% of 1RM every 3-4 without. CG: 2 sessions/week for 50 min. for 15 weeks.	•* pain disability and pain intensity compared to baseline. Beliefs to avoid fear about physical activity just ↓. ↑ ins IID contents (recreation, social activity and occupation).	↑* in the average isometric strength of knee extension and handgrip strength. ↑* in the average amount of duration of physical activity.	The intervention of resistance exercise had a positive effect on recreational, social and occupational disability.
Gavi et al. 2014[15]	Physical conditioning (strength and VO2max), FMS impact score, quality of life questionnaire, depression inventory and HRV.	Group TR: 3 series of 12 reps. in 12 exercises for the whole body; Loads of 45% of 1RM. Flexibility Group (FLEX): Stretching for the whole body. 2 sessions/week for 45 min. for 16 weeks.	•* in pain perception in both groups, but the effect in the RT group was greater than in the FLEX group after 30 days and after 4 months. Improvements * for both groups in function, depression, FM and QOL were observed in both groups. ↑ improvement in anxiety in the FLEX group compared to RT.	↑* higher for FM in the TR group compared to FLEX for all muscle groups. ↑* of fitness, strength and VO2max. in the TR. ↔ in autonomic modulation (HRV) in both groups.	Despite improvements in depression, anxiety and quality of life in both groups, no effect of strength training on autonomic modulation was observed.
Hooten et al. 2012[16]	Peak VO2, pain severity and FM.	GTR: Leg curl, knee extension and biceps thread for 25 - 30 min./day, 10 rep's were performed. with loads ranging from 1 to 3 kg (MMSS) and 3 to 5 kg (MMII), with progressive load increase (1 kg per week). GTA: Stationary bike; Gradual increase in intensity and duration: 10 min./day during the 1st week, with a gradual increase of 5 – 10 min. in the other weeks. Duration: 3 weeks.	^ pain thresholds and ↓* in pain severity from baseline to 3rd week.	↑ of the peak VO2 and in force in the TR group ↑ of VO2 peak higher in AT compared to TR.	↑* in aerobic strength and conditioning occurred during the three-week study period. RT and AT have equivalent effects on pain severity in patients with FMS. Both exercises have favorable effects in adults with FMS.

Continue…

Table 3: Continuation

Author/ year	Variable analyzed	Exercise applied and Weekly frequency/duration	Exercise applied and Weekly frequency/ duration	Biological responses to physical training	Conclusions
Kayo et al. 2012[17]	Pain intensity, visual pain scores, FMS impact score and QoL questionnaire.	TR: 11 exercises, using free weights and body weight. AT: Heating and stretching (5 to 10 min.) + stimulus conditioner and cooling (5 min.) started at 40 to 50% and progressing throughout the week to 60 to 70% of hrr. Every 4 weeks, the duration was increased (from 25 - 30 min. to 50 min.). 3 sessions/week for 60 min. for 16 weeks.	The VAS scores were * higher in the CG compared to THE and RT; ↔ * between the AT and TR groups. The FIQ scores were *↑ in the CG compared to the AT and TR groups. They were *- in the AT group compared to the TR. ↑* in the SF-36 scores for body pain, vitality, general health, social functioning and mental health in the AT and RT groups. For physical functioning and physical function only in the AT group demonstrated ↑*.	Not observed in the study.	Both exercise modalities (RT and AT) provided greater pain relief in patients with FMS than isolated medications or conventional treatment.
Ribeiro et al. 2018[23]	Pain intensity	Exercises: Leg press and supine (I) standard prescription (STD; 3 × 10 repetitions at 60% of maximum strength); (II) self-selected load with fixed number of repetitions (SS); (III) self-selected load with volume load (i.e., × sets × repetitions) combined for STD (SS-VM); and (IV) self-selected load with a free number of repetitions until reaching the score 7 of the perceived effort assessment (SS-RPE).	VAS ↑ immediately after all sessions, and after 48, 72, 96 h, remaining high in relation to the pre-values. ^ SF-MPQ immediately after all exercise sessions and then gradually over time, reaching baseline levels in 24 hours.	Not observed in the study	The prescribed and preferred intensity resistance exercises failed to reduce pain in patients with FMS.
Medeiros et al. 2020	Pain intensity, QOL, sleep quality, catastrophic thoughts about pain, fears and beliefs related to physical and occupational activities.	MPG: performed exercises based on the Mat Pilates method. Each session lasted about 50 min/12 without. 9 exercises performed with progressions each month: 1 series of 8 rep in the first month. Then, they were performed in 2 series of 10 rep in the second month. Finally, they were performed in 3 sets of 8 repetitions in the last month.	FIQ improves in both groups, with MD=1.6 CI95% 1.1/ 2.2 for MPG. Pain improvement assessed by VAS, MD=1.3 95% CI 0.22/2.3 for MPG. The MPG improves in the following domains of the SF-36: vitality (MD=-9.14 CI95% 0.06/18.2), functional capacity (MD=-9.5 95% CI -18.2/-0.06) and pain (MD=-11.5 95% CI -21.0/-2.0). In fabq-phys, improvement in domain activities (MD=4.9 CI 95% 1.6/8.2). The MPG improves in the following domains of the SF-36: vitality (MD= -9.14 CI 95% 0.06/18.2), functional capacity (MD=-9.5 CI 95% -18.2/- 0.06) and pain (MD=-11.5 CI 95% -21.0/-2.0). In FABQ-Phys, improvement in domain activities (MD=4.9 95% CI 1.6/8.2).	Not observed in the study.	The Mat Pilates method and aquatic aerobic exercises were effective after 12 weeks of treatment for patients with FMS in pain improvement.
Carbonell-Baeza et al. 2010[26]	Pain threshold Body composition Physical fitness	Low/moderate swimming, balancing exercises, monopedal/bipedal position changes, coordination, and dance exercises. 3x week/12 weeks	↑ pain threshold at various points in IG after intervention	↑ MMI flexibility	A 3-month multidisciplinary intervention had a positive effect on the pain threshold at various painful points in women with FMS. Although no overall improvement was observed in physical fitness or body composition, the intervention had positive effects on lower body flexibility.

Aerobic Training Group (GTA); Resistance Training Group (GTR); Stretching group (SG); Activity Moderate to Vigorous Physics (MVPA); Increase (↑); Low Intensity Walking (ICB); Nordic Walking (CN); Decrease (↓); Physical Components Scale (ECF); Mental Components Scale (McE); Borg perceived stress scale (PSE); Hospital anxiety and depression scale (HEAD); Visual analog scale (VAS); Visual analog pain scale (VAS); Mean difference (MD); Short McGill pain questionnaire (SF-MPQ); Sophrology Group (GS); Statistically significant (*); Multidimensional tool that mediatises eight domains: physical functioning, physical role, body pain, general health, vitality, social functioning, emotional role and mental health (SF-36); Fibromyalgia syndrome (FMS); Mat Pilates Group (MPG); Confidence interval (CI); Heart Rate (HR); Reserve heart rate (HRR); Intervention group (GI); Control Group (CG); Sophrology Group (GS); Trained Group (GT); Idate Trait-State (IDATE); Pain Disability Index (IID); Beck Inventory (BECK); InventBeck Depression River (IDB); Multidimensional Fatigue Inventory (IMF-20); Questionnaire of beliefs and avoidance of fear(FABQBR); Clinical improvement (CM); Lower Limbs (MMII); Upper Limbs (MMSS); Model Program of Community Health Activities for the Elderly (CHAMPS); Quality of life (Qol); Fibromyalgia Impact Questionnaire - Physical Disability (FIQ-PI); Fibromyalgia Impact Questionnaire, Pain Scale (FIQ, Pain); Impact questionnaire on fibromyalgia (FIQ); Patient Health Questionnaire-8 (PHQ-8); No changes (↔); 6-minute walk test (6MWT); Timed Test (TCN); Maximum Repetition Test (1RM); Aerobic Training (AT); Combined Training (CT); Resistance Training (TR); Heart rate variability (HRV); Updated version of fiq questionnaire (FIQ-A).

Table 4: Outcome from studies related to Biological and psychophysiological responses to Aerobic Training

Author/year	Variable analyzed	Exercise applied and Weekly frequency/ duration	Psychophysiological responses to physical training	Biological responses to physical training	Conclusions
Kkaleth et al. 2013[11]	Number of hours of PA, FMS impact score, health level score, and pain severity.	40-50% of HRR, (10-12 min/session by 2-3 d/ sem). ↑ gradual volume for 55-65% of VHR (28-30 min/ session and 3-4 days/sem.) 2 - 3 sessions/week for 10-12 min; ^ progressive for 3 - 4 sessions/week of 28-30 min./session. SUS-PA: ↑ minimum of 10 MET h/sem. which was maintained or ↑ for another 12 weeks; UNSUS-PA: reached a minimum ↑ of 10 MET h/sem, followed by a decrease in PA; LO-PA: Did not attain a ↑ of at least 10 MET h/sem.	↑ of the participation of individuals in MVPA was related to improvements * in FIQ-PI, PHQ-8 and FIQ-Total. Until week 36, there was a greater improvement* of the FIQ-PI in the SUS-PA and UNSUS-PA groups compared to the LO-PA. * Greater improvement of FIQ-Total for sus-pa and unsus-pa groups compared to LO-PA group. CM * in pain severity of the SUS-PA group compared to the LO-PA group.	Not observed in the study.	↑ participation in MVPA for at least 12 weeks improves FF and general well-being in patients with FMS although the achievement of higher volumes of PA is not associated with worsening of pain.
Mannerkorpi et al. 2010[13]	Impact of FMS, Exercise HR, 6MWT and fatigue inventory.	CN: 9 to 11 on the PSE scale; ^ gradual throughout the exercise ranging from 13 to 15, alternating with low intensity of 10 – 11. Low intensity group (ICB): 9 to 11 on the PSE scale. CN: 2 sessions/week for 20 min. for two 15 weeks. IC: 1 session/week for 20 min. for two 15 weeks.	↔* FIQ PAIN intergroups (CN and IC.) ↑* higher for the change in physical FIQ in the CN group compared to the IC group) (when compared to the base lines with the post-intragroup intervention). ↔* for total FIQ scores in the intragroup analysis of CN and IBC.	↑* higher in the alteration in the 6MWT in the CN group compared to the IC group (when compared to the base lines with the post-intragroup intervention). •* HR in the submaximl exercise test in the CN group compared to the change in the IC group.	CN seems to be a safe option for patients with FMS who wish to improve their functional capacity by exercise, with less risk of pain manifestations.
Hooten et al. 2012[16]	Peak VO2, pain severity and FM.	TR: Leg curl, knee extension and biceps thread for 25 - 30 min./day, 10 rep's were performed. with loads ranging from 1 to 3 kg (MMSS) and 3 to 5 kg (MMII), with progressive load increase (1 kg per week). AT: Stationary bike; Gradual increase in intensity and duration: 10 min./day during the 1st week, with a gradual increase of 5 – 10 min. in the other weeks. Duration: 3 weeks.	↑* of pain thresholds and ↓* in pain severity from baseline to 3rd week.	↑ of the peak VO2 and in force in the TR group ↑ of VO2 peak higher in AT compared to TR.	↑* in FM and aerobic conditioning occurred during the three-week study period. RT and AT have equivalent effects on pain severity in patients with FMS. Both exercises have favorable effects in adults with FMS.
Kayo et al. 2012[17]	Pain intensity, visual pain scores, FMS impact score and QoL questionnaire.	TR: 11 exercises, using free weights and body weight. AT: Heating and stretching (5 to 10 min.) + stimulus conditioner and cooling (5 min.) started at 40 to 50% and progressing throughout the week to 60 to 70% of hrr. Every 4 without, the duration was increased (from 25-30 min. to 50 min.) 3 sessions/week for 60 min. for 16 weeks.	The VAS scores were * higher in the CG compared to THE and RT; ↔ * between the AT and TR groups. The FIQ scores were *↑ in the CG compared to the AT and TR groups. They were *- in the AT group compared to the TR. ↑* in the SF-36 scores for body pain, vitality, general health, social functioning and mental health in the AT and RT groups. For physical functioning and physical function only in the AT group demonstrated ↑*.	Not observed in the study.	Both exercise modalities (RT and AT) provided greater pain relief in patients with FMS than isolated medications or conventional treatment.

Continue…

Table 4: Continuation

Author/year	Variable analyzed	Exercise applied and Weekly frequency/ duration	Psychophysiological responses to physical training	Biological responses to physical training	Conclusions
Sañudo et al. 2015[18]	HRV, pain severity, sleep disorders, stiffness, anxiety and depression.	45 - 60 minutes: 15 to 20 minutes of stationary aerobic exercise, with 60 to 65% of MAX HR. and 15 minutes of interval training between 75 and 60 min. HR max. 80% (six repetitions of 1.5 min, with interpolated rest intervals of 1 min). Duration: 2 sessions/week for 24 weeks.	• anxiety in the AT group compared to the CG. • depression in relation to baseline in the AT group, however, was not statistically different from the change in CG.	↑* in all HRV variables in relation to baseline, however, there was no ↑* when compared to CG.	The AT program induced changes in the modulation of the cardiac autonomic nervous system in women with FMS. These changes in HRV parameters were accompanied by CM in anxiety and depression.
Wang et al. 2018[19]	Overall patient assessment, anxiety and depression, FMS symptoms, confidence recovery, arthritis and QOL self-efficacy	AT: Heating: (15 min, 20 min.) Training: (50-60% of HR. max. estimated (13 and 25 min). ↑ gradual time every two weeks. Weeks 10 to 12: 40 min. (60-70% of the estimated HR). AT: 2 sessions/week. for 24 weeks. Ta i Chi: Protocol adapted for FmS. Tai Chi: Group 1 (n= 39): 1 session/week for 12 weeks; Group 2 (n=37): 2 sessions/week for 12 weeks; Group 3 (n=39): 1 session/week for 24 weeks; Group 4 (n=36): 2 sessions/week for 24 weeks.	Both groups presented CM in the FIQ-A indices, however, there was a higher FIQ-A ↑ for *tai chi* when compared to AT. Overall assessment, HADS Anxiety; self-efficacy and coping strategies had ↑* in the difference of the scores between *the tai chi and* AT groups at 24 weeks. The 24-week tai chi groups had a ^ * improvement of HADS depression scores, Beck II depression inventory, FIQ-A and SF-36 compared to 12-week groups	Not observed in the study.	Compared to aerobic exercise, tai chi seems to be as effective as or better in the treatment of FMS.
Gómez-Hernández et al. 2020[24]	Sleep quality, Qol and pain perception	Moderate-intensity cycling (50%-70% of predicted HRmax for age) three times a week for 12 weeks.	Improvements* in the measurement of 4 without compared to the control group: Pittsburgh Sleep Quality Index; Epworth Sleepiness Scale; Fibromyalgia impact questionnaire (0.93±7.39); and visual analog scale (0.52±0.05). Improvements* compared to the control group: Pittsburgh Sleep Quality Index, Epworth Sleepiness Scale; Fibromyalgia impact questionnaire (1.15±9,11); and visual analog scale (0.81±0.62).	Not observed in the study	Adding stretching to a moderate-intensity aerobic exercise program increased sleep quality, decreased the impact of fibromyalgia on QOL, and reduced pain compared to just one moderate-intensity aerobic exercise program in the sample of women with fibromyalgia.

≥10 MET h wk increment in MVPA and sustained (SUS-PA); Increase (↑); Low Intensity Walking (ICB); Nordic Walking (CN); Decrease (↓); Physical Components Scale (ECF); Low Intensity Walking (ICB); Nordic Walking (CN); Mental Components Scale (McE); Borg perceived stress scale (PSE); Hospital anxiety and depression scale (HEAD); Visual analog scale (VAS); Statistically significant (*); Multidimensional tool that mediatises eight domains: physical functioning, physical role, body pain, general health, vitality, social functioning, emotional role and mental health (SF-36); Fibromyalgia syndrome (FMS); Heart Rate (HR); Reserve heart rate (HrR); Control Group (CG); Trained Group (GT); Idate Trait-State (IDATE); Increase ≥10 MET h/wk in MVPA, followed by decline (UNSUS-PA); Beck Inventory (BECK); Beck Depression Inventory (IDB); Multidimensional Fatigue Inventory (IMF-20); Clinical improvement (CM); Lower Limbs (MMII); Upper Limbs (MMSS); It did not reach a ≥10 MET h/wk in MVPA (LO-PA); Model Program of Community Health Activities for the Elderly (CHAMPS); Quality of life (Qol); Fibromyalgia Impact Questionnaire - Physical Disability (FIQ-PI); Fibromyalgia Impact Questionnaire, Pain Scale (FIQ, Pain); Impact questionnaire on fibromyalgia (FIQ); Patient Health Questionnaire-8 (PHQ-8); No changes (↔); Timed Test (TCN); Maximum Repetition Test (1RM); Aerobic Training (AT); Aerobic exercise (As); Combined Training (CT); Resistance Training (TR); Heart rate variability (HRV); Updated version of the FIQ questionnaire (FIQ-A); Moderate-vigorous physical activity (MVPA); General variability (TP); 6-minute walk test (CT-6); Low frequency (LnLF); mean square root of successive R- R intervals (rMSSD); High frequency(LnHF); Hospital anxiety and depression scale (HADS).

being involved in neurotropic and neuroprotective signaling of the hippocampus.

Another interesting finding was that RT promoted an increase in pain threshold. In fact, Hooten et al.[16], compared the effects of RT vs. AT, and observed that regardless of the methodology applied, the results were equivalent in some aspects, including the pain threshold. The explanation may be due to the effects of PE on peripheral and central sensitization in patients with FMS. We can also attribute this finding to the effects of exercise on sensitization of peripheral mechanoreceptors and the improvement

Table 5: Biological and Psychophysiological Responses to Concurrent Training

Author/Year	Variable analyzed	Exercise applied/ weekly frequency and duration	Psychophysiological responses to physical training	Biological responses to physical training	Conclusions
Sañudo et al. 2010	Maximum power in the middle of the squat; Number of squat repeats in 60 s; Fatigue index; FIQ and SF-36.	IG: EA (4-6 sets from 2-3 min to 50 - 69% HR MAX and 1-2 min rest between sets); Flexibility (1-3 sets of 8-9 stretching exercises with 30 sec duration) ER (8 exercises a series of 8-10 repetitions for the main muscle groups with 1-3kg) Vibration protocol (on vibratory platform 3 series of 45 sec with interval of 120 sec and 4 series of 15 sec,all at a frequency of 20Hz and variable amplitude of 2-3 mm) 3 times a week ± 60min CG: EA (4-6 sets from 2-3 min to 50 - 69% HR_{MAX} and 1-2 min rest between sets); Flexibility (1-3 sets of 8-9 stretching exercises with 30 sec duration). ER (8 exercises a series of 8-10 repetitions for the main muscle groups with 1-3kg) 3 times a week ± 60min.	↑* Qol, vitality and mental health (measured by SF-36) compared to baseline. ↑* in FIQ physical functioning	↑* in the number of squats relocated in 60s.	Both groups obtained gains for the analyzed variables, there was no significant difference between the groups.
Sañudo et al. 2012	QoL, FM Ssymptoms, symptoms of depression and aerobic fitness.	2 times by no durations of 45 to 60 min for 6 months. 10 to 15 min of EA from 65% to 70% of HR max, 15 to 20 min of strengthening exercises (a series of 8-10 rep for 8 different muscle groups, load of 1-3 kg).	Melhora* for the TG on the CG in the FIQ scores, (F [1,34]=20.618, n^2=0.377) at the time point of 6 months. improvements* within the group for the TG in fIQ (F[5,8]=8.663, n^2=0.419), the SF-36 (F[5,8]=8.055, n^2=0.402), and the BDI (F[5,7]=8.067, n^2=0.423).	Not observed in the study	A long-term exercise program can produce immediate improvements in key health areas in women with fibromyalgia.
Sañudo et al. 2015[18]	Qol and depression.	EA: 10-15 min of aerobic exercise at 65-70% of HRmax at an intensity of 60-70% of predicted HRmax and adjusted for age 2 or 3 times a week. PE: 8-season circuit. The 8 muscle groups: shoulders (deltoid and biceps), neck (trapezoid), hip (gluteus and quadriceps) and back-torso (large dorsal, pectoralis major, abdominal).	* improvements in health status and functional capacity for the exercise group in relation to the control group. The size of the effect (95% CI) for the FIQ was 0.58 (-14.12, -2.35) for the SF-36. Overall score: 0.54 (1.28, 14.52) and in the mental health domain of the SF-36: 0.51 (1.20, 16.26).	Not observed in the study	Combination of aerobic exercises, strengthening and flexibility in the long term improves psychological health status and health-related Qol in patients with FMS.
Sauch Valmaña et al. 2020	Pain intensity and QOL	Aerobic resistance and strength work, 2 days/without for a period of 12 without, with each session lasting 90 minutes.	No significant results observed	Not observed in the study	A low intensity exercise program 2 days a week over a 12-week period had no significant effect on pain, perceived health status, and the impact of the condition on a sample of women with FMS.

GI: intervention group; CG: control group; Maximum heart rate (HRmax); Impact questionnaire on fibromyalgia (FIQ); Patient Health Questionnaire-8 (PHQ-8); Beck Inventory (BECK); Beck Depression Inventory (IDB); Multidimensional Fatigue Inventory (IMF-20); Clinical improvement (CM); Resting heart rate (HRF); Quality of life (Qol); Confidence interval (CI); Training group (GT); Fibromyalgia syndrome (FMS); Multidimensional tool that mediatises eight domains: physical functioning, physical role, body pain, general health, vitality, social functioning, role and mental health and mental health (SF-36); Aerobic Exercise (As); Physical Exercise (PE); Resistance Exercise (ER); Physical Activity (PA).

of dysfunction in the central modulation of pain. Assumpção et al.[9], submitted the study participants to 2 sessions of RT and stretching sessions for 12 weeks for 40 minutes, and observed an increase in the threshold of pain, corroborating other studies in the literature[32,33].

FMS leads to metabolic and oxygenation alterations in muscle fibers, in addition to painful hypersensitivity attributed to uncoordinated action of nociceptive and pain inhibition mechanisms, resulting in sensory distortion. In turn, RT leads to an improvement in the molecular metabolic status of skeletal muscle, due to stimulation promoted by muscle contraction, in addition, RT can also increase the concentration of myoglobin, softening muscle hypoxia.

Increased quality of life

The pathophysiology of FMS in addition to pain also leads to decreased levels of serotonin and endorphin[34]. It is also common for sleep disorders caused by electroencephalic disorders and anxiety disorders. The absence of the complete sleep cycle impacts a smaller restorative effect, which ultimately results in a significant reduction in quality of life and decreased productivity during the day[35].

The studies analyzed in this review observed a significant increase in the quality of life of individuals who participated in the intervention with RT. For example, the study by Gavi et al.[15], showed that after RT for 16 weeks, there were improvements in scores of quality of life, anxiety, depression, in addition to decreased pain perception.

Based on the findings analyzed, interventions made in groups can benefit the quality of life of this population, as it would bring important benefits, such as integration and greater social interaction, also allowing greater motivation for the regular practice of PE.

Resistance exercise and biological variables

In the studies that addressed RT and muscle strength were evaluated, positive responses were found, such as strength increases. Silva et al.[10], Larsson et al.[12] and Gavi et al.[15] used strength training for the whole body. This type of approach can be a factor that facilitates the adhesion to training to these individuals, allowing fewer training sessions during the week to obtain significant gains in muscle strength, which is related to good performance in activities of daily living. However, it is necessary to make reservations, in the sense that if this training methodology is adopted, the recovery time has to be well dosed, to allow tissue regeneration in these individuals.

In the study by Hooten et al.[16], VO2 was analyzed, obtaining positive responses in the face of an intervention of resistance exercises, with concomitant increases in strength and reductions in the severity of pain, contributing to positive responses in quality of life. Corroborating the aforementioned analysis, in the meta-analysis by Busch et al.[36], patients with FMS obtained reductions in fatigue in the intervention of resistance exercises, and this variable was influenced by strength increases and reduction of muscle pain.

Aerobic exercise and psychophysiological variables

Pain severity and intensity were analyzed in the studies by Hooten et al.[16] and Kayo et al.[17], and in both there were no differences between PE and RT groups. These studies showed similar results regarding pain. Both training methods stimulated equivalent improvements in pain.

Responses in sleep performance and depression and anxiety of individuals were also found in the study by Gómez-Hernández et al.[24], positive sleep responses were found in the face of moderate intensity cycling and Sañudo et al.[18], found reductions in anxiety and depression levels from aerobic exercises that included walking and running.

These findings indicate that when the goal of training is to improve the pain outcome, the patient's preference should be considered, since the benefits are similar, but the conditions of sleep, anxiety and depression are positively influenced by aerobic training. Therefore, we recommend the periodization of the two types of stimuli in the training program as a way to vary the type of stimulus of PE.

Aerobic exercise and biological variables

With regard to cardiorespiratory conditioning, only in the study by Hooten et al.[16], VO2 (peak) was evaluated before and after PE, showing greater increases in this variable, compared to the RT group, emphasizing the importance of performing this training method for gains in cardiorespiratory fitness of patients, and these results were obtained, concomitantly with decreases in pain severity.

Mannerkorpi et al.[13], found a significant reduction in heart rate in a submaximal exercise test for the group that did Nordic walking when compared to the low intensity walking group. This finding indicates that exercises that do not promote a considerable level of overload in the cardiovascular system are insufficient to promote cardiovascular improvements in these individuals, and therefore, the progressive increase in intensity should be stimulated.

Practical considerations for the prescription of physical exercise in FMS

For an adequate prescription of physical exercises in this population, it is necessary to consider that these people are subjected to a chronic perception of pain. This in itself is already characterized as an important barrier to the practice of physical exercises. Moreover, from the physiological point of view, PE itself is a stressful stimulus for an organism already affected by stress[37].

Therefore, it is necessary to carefully think about the volume and intensity of training for these individuals.

The exercise prescription should be based on the biological individuality of each subject, so the performance of physical tests helps to prescribe the exercise more accurately and assertively. The one-repetition maximum (1RM) test - used as the gold standard for muscle strength determination[38], seen in the articles by Silva et al[10] and Larsson et al.[12], the VO2max test, which is the maximum capacity of an individual to absorb, transport and consume oxygen, being an excellent predictor of aerobic performance, seen in the articles by Gavi et al.[15] and Hooten et al.[16] and CT-6, a 12-minute cooper walk test adaptation that assesses the relationship between physical fitness and maximum oxygen consumption[39], seen in Mannerkorpi et al[13] and Sañudo et al.[21] are some of the examples.

According to the findings, the load and intensity appropriate for prescription of RT revolve around 1 to 3 sets of 8 to 15 repetitions that include 8 to 12 whole body exercises, using 40% to 80% (progressive loads per week) of 1RM twice a week. The prescription of AT is around 40 to 50% of the heart rate reserve (HRR) with a gradual increase in volume to 55 to 65% or 40% to 70% of the estimated maximum heart rate (MHR) from 10 to 60 min/session for 2-3 per week, ranging from running on the treadmill or stationary bike. Furthermore, variations in prescription parameters were found in the findings, for example, in the study by Mannerkorpi et al.[13], the Physical Self-Efficacy (PSE) scale alternated between grades 9 to 11 was used with gradual increase throughout the exercise ranging from 13 to 15.

Study limitations

The time frame adopted by the 10-year study optionally determined by the authors was based on the question of the development of more current evidence related to the treatment of FMS, but this cut-out may make it impossible to make a general analysis of the characteristic condition of the disease, from its discovery to the current scenario.

Conclusion

Considering the findings of this systematic review, popular training alternatives such as RT, AT and CT should be encouraged for this population, because in addition to being low-cost interventions, they offer significant improvements, both biological (increased pain threshold, decreased sensitive points, increased muscle strength, improvement of cardiorespiratory fitness) and psychophysiological (symptoms, quality of life, vitality and mental health) contributing significantly to the improvement of pain. However, it is worth mentioning that exercises should be individualized by qualified professionals who are aware of the appropriate volume and intensity for the individual, considering the physiological stress that the syndrome imposes on these people.

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