Effect of Moderate-Intensity Exercise on Inflammatory Markers Among Postmenopausal Women

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Background: Declines in ovarian function in postmenopausal women may contribute to increase inflammatory cytokines, which can lead to chronic diseases. However, studies have shown that exercise interventions are important to manage inflammatory conditions. Thus, the objective of this study was to analyze the effect of exercise intervention on inflammatory markers among obese and postmenopausal women. **Methods:** 70 women composed the sample (Exercise group [EG; n = 35] and nonexercise group [nEG; n = 35]). IL-6, TNF-α, and IL-10 were the inflammatory markers analyzed. Exercise program was 20 weeks long and consisted of aerobic and neuromuscular training. Data about chronic diseases, medication use, dietary intake, body composition and biochemical variables were collected. **Results:** EG showed significant reductions in body mass index, waist circumference and body fat percentage, as well as increased lean body mass. EG showed significant reductions in TNF-α and significant interaction between group and intervention time. Reductions in IL-10 were identified only in nEG. Substantial effect of exercise intervention was observed with increased ratio of IL-10/IL-6 and IL-10/TNF-α. **Conclusions:** Combination of aerobic exercise and resistance training was effective in reducing inflammation. Thus, implementation and maintenance of similar exercise programs can contribute to reduce chronic inflammation among obese postmenopausal women.

Keywords: public health, obesity, chronic disease

Scientific evidence has shown that declines in ovarian function in postmenopausal women may contribute to an increase in inflammatory cytokines,[1,2] and this chronic low-grade inflammation is associated with the pathogenesis of several chronic diseases.[3] However, studies have found that reduction in body fat, as well as body mass index, can decrease inflammatory processes, suggesting that exercise and dietary interventions are important therapeutic tools to manage inflammatory conditions.[4,5]

The impact of exercise on reducing inflammatory markers or increasing anti-inflammatory markers has been investigated mainly through cytokines, such as interleukin-6 (IL-6), tumor-α necrosis factor (TNF-α), and interleukin-10 (IL-10).[3] However, when considering the specific population of overweight and obese postmenopausal women, it is unclear whether improvements on inflammation is due to exercise intervention itself or weight loss associated with exercise program.[6,7] In addition, factors like type of exercise, intensity and duration of intervention appear to interfere

significantly on how exercise can modify concentration of IL-6, TNF-α, and IL-10.[2,6–12]

In Brazil, it has become more common the existence of exercise programs within Health Care Units of the Brazilian National Health System.[13] Although these interventions have focused on the reduction of cardiovascular risk factors (as preventative actions in primary and secondary care levels), not much is known about the potential of these exercise programs on decreasing low-grade inflammation in postmenopausal women. Thus, the objective of this study was to analyze the effect of an exercise intervention (based on the recommendations of the American College of Sports Medicine[14]) on inflammatory and anti-inflammatory modifications among obese and postmenopausal women.

Methods

Sample

The sample was composed of 70 women (age between 50 and 79 years old), users of a Family Health Program unit in the city of Marília, São Paulo state. At the time of data collection, the unit had a record of 786 women with age ≥ 50 years old, and 140 of them were selected randomly for home visiting and invitation to take part in the study.

After the home visit, 94 women agreed to participate in the study, but only 82 met the inclusion criteria, defined as i) had experienced at least 12 consecutive months without menstruation, ii) percentage of body fat (%BF) ≥ 35% (diagnosis of obesity),[15] iii) accumulation of less than 150 minutes per week of moderate-to-vigorous exercise in the past 6 months, and iv) no physical limitations and medical restrictions for participating in exercise intervention. Smoking habit (currently or in the past), the use of hormone replacement therapy and/or anti-inflammatory medication were considered exclusion criteria.

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Participants were randomly assigned to exercise group (EG; n = 44) and nonexercise group (nEG; n = 38). At the end of the study, 9 women in the EG and 3 from the nEG were excluded due to i) health problems limiting the engagement in the exercise program; ii) health problems associated with inflammation, such as flu, acute pain related to arthritis, or other health-related issues that happened during data collection period; iii) have completed less than 65% of the exercise program; and iv) have missed days of assessments. The nEG was instructed to maintain their normal routine (physical activity and eating habits).

Before implementation, the study was approved by the Research Ethics Committee (protocol number 364/2011), the Municipal Committee of Evaluation and Research (COMAP) (process number 476/11-SS), and the Brazilian Registry of Clinical Trials (REBEC) (process number RBR-8fdmb8).

Independent Variables

To avoid bias, interviews and physical assessments were conducted by independent researchers who did not know in which group the participants were assigned. Data about chronic diseases, medication use and postmenopausal period were collected through interviews and confirmed in the medical records of each participant. All assessments were performed before and after the intervention period for both groups (EG and nEG).

Dietary intake was assessed with a 24-hour recall providing estimates of daily caloric intake (DCI), resting metabolic rate (RMR) and energy balance (EB). EB was calculated as the difference between RMR and DCI.[16]

Lean body mass and body fat were estimated by bioelectrical impedance analysis, using specific equations for postmenopausal women.[17] Obesity was defined as percentage of body fat ≥ 35%.[15] Body mass index (BMI) was calculated using measurements of weight and height and obtained by dividing weight by squared height (kg/m^2). Waist circumference (WC) measurements were performed to assess abdominal obesity.

Peak oxygen uptake (VO_2peak) was predicted using the Rockport 1-mile walking test.[18] For participants using beta-blocker medication, the heart rate (HR) was adjusted according to the dosage and type of medication.

Biochemical Measurements

To collect blood samples, all participants were instructed to fast for at least 12 hours, do not perform any physical activity in the previous 24 hours and do not drink alcohol beverages 72 hours before the test. The measurements included proinflammatory cytokines (IL-6 and TNF-α) and anti-inflammatory cytokine (IL-10). The cut-off points for each inflammatory marker were set as follows: IL-6 > 2.05 pg/mL;[19] TNF-α > 2.30 pg/mL;[20] IL-10 > 3.5 pg/mL.[21] Cytokine levels were measured using the Enzyme-Linked Immuno-Sorbant Assay (ELISA) Kit (BD Biosciences) with detection limit of 2.0 pg/mL for TNF-α and IL-10, and 2.2 pg/mL for IL-6. The ratios between IL-10 and TNF-α (IL-10/TNF-α) and IL-10 and IL-6 (IL-10/ IL-6) were calculated to analyze the rate of synthesis between anti-inflammatory and inflammatory cytokines.[22]

We also performed measurements of fasting blood glucose (BG), total cholesterol, high-density lipoprotein (HDL-C), low-density lipoprotein (LDL-C), and triglycerides (TG). Plasma concentration of total cholesterol and TG were assessed by enzymatic colorimetric method; HDL-C by selective inhibition; LDL-C by Friedewald's formula (triglyceride levels below 400 mg/dL); and

very low-density lipoproteins (VLDL-C) by the equation: TG/5. BG was estimated by glucose oxidase method. Creatine kinase (CK) activity was determined using the CK-NAC Kit ultraviolet AA (Bioclin), which was used as a measure of muscle injury (upper reference limit for women = 140 U/L).

Exercise Program

The exercise program was 20 weeks long, divided into 3 weekly sessions of 75 minutes each, accumulating 225 minutes per week. The sessions were divided into i) blood pressure measurements and warm-up activities (10 minutes), ii) neuromuscular training (25 minutes), iii) aerobic training (50 minutes), and iv) cool-down activities (5 minutes). The exercise program followed the recommendations proposed by the American College of Sports Medicine.[14,23]

Main Part 1: Neuromuscular Training. Neuromuscular training was composed of 3 parts: stretching, isometric and dynamic exercises. Stretching consisted of 6 exercises performed in 2 sets of 30-second repetitions: 2 for the lower limbs, 2 for the upper limbs, 1 for the neck and 1 for the lower back. Isometric part consisted of, initially, 4 exercises performed in 4 sets (4 seconds of submaximal contraction followed by 30 seconds of recovery), with progression every 4 weeks [increase in the number of exercises (up to 6 types) or reduction of recovery time (down to 10 seconds)]. Dynamic part consisted of, initially, 3 exercises performed in 4 sets (10 repetitions followed by 30 seconds of recovery), with progression every 4 weeks [increase in the number of exercises (up to 6 types) or reduction of recovery time (down to 10 seconds)].

Main Part 2: Aerobic Training. Aerobic training consisted of walking on a flat surface with intensity of 50% to 60% of VO_2peak, estimated by the Rockport 1-mile walking test.[18] This test is designed for people aged 30 to 69 years old, both sexes, and includes in its equation values of body weight (kg), age (years), sex, time (minutes) to cover the distance of 1600 m, and heart rate (HR) at the end of the test. The percentage values of VO_2 were converted into walking speed (meters per minute) according to the metabolic equation described in the ACSM's Guidelines for Exercise Testing and Prescription.[24] Then, considering the conversion into walking speed, we estimated the minimum and maximum distance to be walked during 50 minutes. We also monitored the percentage of heart rate reserve (%HRR). The maximum heart rate (HR max) was estimated using the equation for asymptomatic women aged 35 to 85 years proposed by Gulatti and colleagues.[25]

Statistical Analyses

Considering the average standard deviation of 1.5 pg/mL, study power of 80% and 5% significance value, the sample size was initially estimated in 36 sampling units to detect a difference of 1 pg/mL for IL-6 values. At the end of the study, considering a mean difference of 1.36 pg/mL, mean standard deviation of 1.55 pg/mL and sample size of 35 sampling units per group, it was estimated a study power of 96%. The results were reported as mean and 95% confidence interval (95% CI). The normal distribution was analyzed by the Kolmogorov-Smirnov test and Lilifors correction. Delta percentage changes were calculated as follow: $\Delta\% = [postpre] \times 100/pre$. To analyze the differences of $\Delta\%$, a *t* test for independent samples was performed. Repeated-measures ANOVA (Split plot) analyzed the effect of interaction between group and time of intervention. The Box's M test was used to verify if the covariance matrices of the observed dependent variables were the same for both

groups. Mauchly's test was used to test the hypothesis of sphericity. In the case of rejection of the sphericity assumption, the analysis was based on the Greenhouse-Geisser multivariate test. Variation in WC, BMI, and %BF were treated as potential confounders in the analysis of repeated-measures ANOVA. Significance was set at 5% and analyzes were performed using SPSS software, version 19.0 for Windows.

Results

The participants were initially classified as sedentary, presenting average of 41 ± 58 minutes of moderate exercise per week. EG and nEG showed no significant differences for age (61.3 ± 6.4 *vs.* 59.8 ± 7.1 years old; *P* = .342), and time without menstruation (164.5 ± 93 *vs.* 157.4 ± 108 months; *P* = .768). At the end of the study, the adherence rate in the intervention was 77.1 ± 10.4%.

EG and nEG presented no differences according to diagnosis of hypertension (74% *vs.* 66%), dyslipidemia (63% *vs.* 54%), osteoporosis (46% *vs.* 43%), arthritis (26% *vs.* 26%), osteoarthritis (17% *vs.* 26%), and type 2 diabetes (26% *vs.* 20%). There were no significant variations of DCI and EB within or between groups, but the EG showed a significant reduction in RMR due to decrease of body weight (Table 1).

EG showed significant reductions in body mass, BMI, WC, and %BF, as well as increased lean body mass. Repeated-measures ANOVA test indicated a significant interaction between group and time of intervention, confirming the significant effect of exercise in body composition variables in the EG (Table 2). Variations (Δ%) of BMI, WC, and %BF were included as covariates and showed no significant effect on Δ% of the cytokines analyzed.

Regarding concentrations of biochemical variables, EG showed significant reductions in total cholesterol, TG, LDL-C, and VLDL-C, as well as a significant interaction between group and time of intervention. Although there was no significant reduction in BG values in the EG, the intervention contributed to maintain it within normal levels, different from the nEG, which showed a significant increase in BG. The effect of the exercise program on glycemic control can be confirmed by the significant interaction between group and time of intervention. There were no significant changes in HDL-C and CK (Table 3).

Although the average percentage variation (Δ%) of EG indicated reductions in IL-6 values, no significant differences and no interaction were found between groups. On the other hand, EG showed significant reductions of TNF-α values and significant interaction between group and intervention time. Significant reductions of IL-10 were identified only in nEG, as well as interaction between group and time of intervention, highlighting the protective effect of exercise in maintaining the concentrations of this anti-inflammatory cytokine. Regarding the balance between inflammatory and anti-inflammatory cytokines, a significant effect of exercise intervention was observed, with increased ratio of IL-10/IL-6 and IL-10/TNF-α (Table 4).

Discussion

This intervention study aimed to analyze the effect of exercise on inflammatory markers among obese and postmenopausal women and results indicated a potential effect of exercise on IL-6, since the EG showed a significant increase in the IL-10/IL-6 ratio, even after reductions of IL-10. In addition, the reduction of IL-10 in the nEG affected the synthesis of anti-inflammatory and proinflammatory cytokines (analyzed by the ratios IL-10/IL-6 and IL-10/TNF-α), showing increased low-grade chronic inflammation in the nEG.

Studies examining the effects of exercise among postmenopausal obese women indicate differences between exercise and control groups mainly because of the worse condition of the control group, even in short-term interventions. Therefore, when studies involve exercise and participants with chronic diseases, results indicating maintenance of medical condition after the intervention should be considered a positive effect of exercise, especially when the control group presents a significant deterioration of biomarkers. The persistent rise of metabolic rate due to chronic diseases can be harmful and lead to a faster progression of health issues, which is associated with energy shifts to other homeostatic mechanisms, associated with an increased catabolic state.[26]

Although the effect of exercise in reducing inflammation is strongly associated with the decrease of body mass and body fat,[6,7,27] we found no significant changes in the cytokines analyzed. This finding indicates that the cytokines modifications observed in this study are, in part, due to exercise intervention.

The strong relationship between adipose tissue and inflammation is explained by the capacity of adipokines (paracrine, autocrine, and endocrine) in affecting the metabolic functions of other tissues. Excessive adipose tissue can have a major impact on the physiological homeostasis of the body, which includes a systemic inflammatory burden.[3,5,6,28]

Although experimental models suggest that exercise might independently cause modifications on blood levels of inflammatory biomarkers by increasing IL-6,[29] part of intervention studies still attribute the improvement of inflammation to reduction of body mass and body fat.[27,30,31] However, a study with 12 weeks of resistance training (moderate / high intensity) observed acute increase in IL-6 concentrations, chronic reduction in TNF-α and chronic increase in IL-10 after the intervention period.[12]

The increase of IL-6 production is considered an important key that explains the chronic effect of exercise on inflammation. However, at rest, IL-6 synthesis is mediated by TNF-α, which explain significant changes in TNF-α and not in IL-6 during short-term intervention studies.[32,33]

A potential mechanism explaining the effect of exercise on reducing inflammation is the decrease in the expression of toll-like receptor 4 (TLR4). In addition, exercise may also increase the anti-inflammatory actions of the melanocortin system associated with the expression of the melanocortin receptor 3 (MC3R).[12]

Although it is known that exercise is beneficial for many reasons, the role of exercise on the modulation of the endocrine function of adipose tissue is only partially clarified, with some studies showing improvement of endocrine fat profile, while others not.[9,34]

Even with a strong association between IL-6 and adipose tissue, IL-6 produced and released into the bloodstream by skeletal muscles during exercise cause positive results because it acts on the adipose tissue inducing lipolysis and adjusting the transcription of genes in abdominal fat.[29] In addition, IL-6 associated with exercise presents an anti-inflammatory effect, mediating the release of IL-1RA and IL-10, which can reduce the synthesis of TNF-α.[35]

Thus, exercise has anti-inflammatory effect and high levels of IL-6 and IL-10 in the circulation (during and after exercise) play a key role in this process.[29,32,36,37] However, the anti-inflammatory effect of exercise is most evident when pathological conditions are present,[37] which indicates the importance of baseline values[10] on the modifications caused by exercise intervention. In addition, TNF-α also regulates IL-6 expression, so reductions in TNF-α may also affect reductions in IL-6.[11,33]

Table 1 Mean, 95% Confidence Interval (95% CI) and Percentage of Variation (Δ%) of Daily Caloric Intake, Resting Metabolic Rate, and Energy Balance in the Exercise and Nonexercise Groups Before and After Intervention (n = 70; Marilia, SP, Brazil)

	EG		nEG		Δ%		Interaction
	Before	After	Before	After	EG	nEG	P-value
DCI	1431 (1352, 1509)	1545 (1434, 1656)	1383 (1259, 1507)	1467 (1346, 1588)	9.57 (1.16, 17.9)	9.31 (0.48, 18.1)	0.768
RMR	1401 (1350, 1453)	1358 (1332, 1439)	1427 (1380, 1475)	1431 (1383, 1479)	−1.19 (−1.80, −0.58)	0.20 (−0.34, 0.85)*	0.681
EB	143 (13, 273)	160 (28, 291)	40 (−94, 174)	36 (−98, 171)	−11 (−36, 13)	12 (−11, 36)	0.681

Abbreviations: EG, exercise group; nEG, nonexercise group; DCI, daily caloric intake (kcal/day); RMR, resting metabolic rate (kcal/day); EB, energy balance (kcal/day).

* Difference statistically significant between groups ($P < 0.05$).

Table 2 Mean, 95% Confidence Interval (95% CI) and Percentage of Variation (Δ%) of Anthropometric and Body Composition Variables in the Exercise and Nonexercise Groups Before and After Intervention (n = 70; Marilia, SP, Brazil)

	EG		nEG		Δ%		Interaction
	Before	After	Before	After	EG	nEG	P-value
BM (kg)	77.3 (72.4, 81.6)	75.6 (70.9, 80.3)	79.4 (74.8, 84.0)	79.7 (75.0, 84.5)	−1.8 (−2.9, −0.8)	0.4 (−0.5, 1.5)*	0.004**
BMI (kg/m²)	30.6 (28.9, 32.4)	30.1 (28.3, 31.9)	32.8 (31.1, 34.5)	32.9 (31.1, 34.8)	−1.7 (−2.9, −0.6)	0.2 (−1.2, 1.7)*	0.039**
WC (cm)	94.3 (90.2, 98.5)	89.6 (85.5, 98.5)	96.9 (92.8, 101.1)	96.6 (92.5, 100.8)	−4.8 (−6.5, −3.1)	−0.2 (−2.1, 1.7)*	0.0001**
LM (kg)	34.5 (32.6, 36.3)	34.6 (32.7, 36.5)	35.9 (34.0, 37.7)	34.8 (32.9, 36.7)	0.3 (−1.2, 2.0)	−2.9 (−4.5, −1.3)*	0.004**
%BF	54.8 (53.4, 56.1)	53.7 (52.1, 55.3)	54.5 (53.2, 55.9)	56.1 (54.5, 57.7)	−1.9 (−3.5, −0.4)	2.8 (1.2, 4.3)*	0.0001**
VO₂peak	18.3 (16.6, 19.8)	22.1 (20.3, 24.0)	16.3 (15.2, 17.4)	18.5 (16.8, 20.2)	24.3 (14.7, 33.9)	14.3 (5.9, 22.6)	0.083

Abbreviations: EG, exercise group; nEG, nonexercise group; BM, body mass; BMI, body mass index; WC, waist circumference; LM, lean mass; %BF, percentage of body fat; VO₂peak, peak oxygen uptake (ml/kg/min).

* Difference statistically significant between groups ($P < 0.05$); ** Interaction statistically significant between group and intervention time (repeated-measures ANOVA).

Table 3   Mean, 95% Confidence Interval (95% CI) and Percentage of Variation (Δ%) of Biochemical Variables in the Exercise and Nonexercise Groups Before and After Intervention (n = 70; Marilia, SP, Brazil)

	EG		nEG		Δ%		Interaction
	Before	After	Before	After	EG	nEG	P-value
BG (mg/dL)	94 (87, 100)	96 (88, 104)	97 (91, 104)	113 (105, 120)	4.4 (−3.6, 12.4)	16.9 (8.2, 25.7)*	0.024**
TC (mg/dL)	213 (202, 224)	208 (195, 220)	205 (194, 224)	216 (203, 228)	−2.2 (−6.2, 1.6)	5.8 (0.4, 11.2)*	0.027**
TG (mg/dL)	145 (123, 167)	119 (101, 137)	149 (127, 171)	159 (141, 177)	−9.9 (−21.4, 1.5)	13.4 (0.9, 25.8)*	0.004**
HDL-c (mg/dL)	53.5 (49.5, 57.5)	53.3 (49.4, 57.2)	53.5 (49.5, 57.5)	50.2 (46.3, 54.1)	0.7 (−4.3, 5.7)	−4.6 (−10.6, 1.2)	0.132
LDL-c (mg/dL)	135 (125, 145)	130 (119, 142)	122 (112, 132)	133 (122, 145)	−1.5 (−8.8, 5.8)	12.8 (2.4, 23.2)*	0.043**
VLDL-c (mg/dL)	29 (24, 33)	23 (20, 27)	29 (25, 34)	31 (28, 35)	−9.9 (21.4, 1.5)	13.4 (0.9, 25.8)*	0.003**
CK (U/L)	101 (87, 116)	102 (90, 114)	96 (82, 116)	90 (77, 102)	8.1 (−7.8, 24.1)	0.5 (−10.6, 11.8)	0.347

Abbreviations: EG, exercise group; nEG, nonexercise group; BG, blood glucose; TC, total cholesterol; TG, triglycerides; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; VLDL-c, very low-density lipoprotein cholesterol; CK, creatine kinase.

* Difference statistically significant between groups ($P < 0.05$); ** Interaction statistically significant between group and intervention time (repeated-measures ANOVA).

Table 4   Mean, 95% Confidence Interval (95% CI) and Percentage of Variation (Δ%) of Inflammatory Markers in the Exercise and Nonexercise Groups Before and After Intervention (n = 70; Marilia, SP, Brazil)

	EG		nEG		Δ%		Interaction
	Before	After	Before	After	EG	nEG	P-value
IL-6 (pg/mL)	4.3 (3.3, 5.36)	2.7 (2.5, 3.3)	3.5 (2.7, 4.3)	3.4 (1.8, 4.9)	−6.0 (−32.5, 20.4)	4.9 (−21.3, 31.2)	0.161
TNF-α (pg/mL)	9.9 (8.4, 11.5)	6.5 (5.2, 7.8)	8.0 (6.5, 9.6)	9.3 (7.4, 11.1)	−23.2 (−41.4, −4.9)	29.0 (4.7, 53.4)*	0.0001**
IL-10 (pg/mL)	10.7 (9.4, 12.0)	8.9 (7.8, 9.9)	17.2 (13.8, 20.6)	8.8 (7.9, 9.7)	−6.1 (−24.0, 11.7)	−35.6 (−49.0, −22.2)*	0.007**
IL-10/IL-6	3.6 (2.7, 4.5)	3.7 (3.1, 4.3)	6.3 (4.4, 8.1)	3.5 (3.1, 4.0)	52.3 (12.7, 91.8)	−14.5 (−39.7, 10.7)*	0.029**
IL-10/TNF-α	1.6 (1.0, 2.2)	2.0 (1.4, 2.6)	3.1 (2.3, 3.9)	2.0 (1.1, 2.0)	87.6 (14.2, 160.9)	−30.5 (−55.8, −5.2)*	0.001**

Abbreviations: EG, exercise group: nEG, nonexercise group; IL-6, interleukin 6; TNF-α, tumor-α necrosis factor; IL-10, interleukin 10.

* Difference statistically significant between groups ($P < 0.05$); ** Interaction statistically significant between group and intervention time (repeated-measures ANOVA).

Taking into account the cut-off points adopted in our study, 77% of the participants in the EG had elevated IL-6 values *versus* 71% in the nEG. Regarding TNF-α, 91.4% of participants in the EG showed high values compared with 88.6% in the nEG. In a study that examined the effect of exercise intervention (6 months) combined with dietary restriction in obese postmenopausal women, with and without metabolic syndrome (MetS), it was observed significant reductions in IL-6 among participants with and without MetS. Both groups showed substantial reductions in %BF and WC, and the significant modifications in IL-6 and TNF-α were associated to the group with higher baseline values.[10]

Important key factors that can influence the anti-inflammatory effect of exercise are: intensity, type, volume, and duration of the intervention,[11] but the ideal amount of exercise to produce meaningful improvement on inflammatory markers is still not fully cleared, mainly in populations with comorbidities.[9]

When comparing the effect of 12 months of intervention with aerobic exercise, diet or diet + aerobic exercise, Imayama and colleagues[27] observed significant reductions in IL-6 in the diet and diet + exercise groups, and modifications were associated with the decrease of body weight. In this study, aerobic exercise at moderate intensity produced no significant reductions in IL-6 after 12 months of intervention.

Similarly, Beavers and colleagues,[6] after 12 months of intervention with moderate-intensity aerobic exercise (150 minutes per week) observed positive effect on IL-6, but this effect was attenuated after adjustment for modifications in adiposity, suggesting that the reduction of inflammatory biomarkers were associated with reduction of body weight.

Another intervention study with 12 weeks of aerobic exercise (60% RHR), strength training, or a combination of aerobic and strength training, showed reductions in TNF-α levels within the groups and when compared with the control group, but no significant differences between the type of intervention and no effect on IL-6. The authors found a significant and positive correlation between TNF-α and reduction of body and visceral fat.[11]

On the other hand, when analyzing the effect of 12 months of low-intensity aerobic exercise, high-intensity aerobic exercise, or combination of aerobic and high-intensity resistance training, Balducci and colleagues[9] detected significant reductions in IL-6 and TNF-α for the group that performed aerobic exercise and resistance training. The group performing high-intensity aerobic exercises also showed significant reductions in IL-6, but not TNF-α.

These findings indicate that a higher volume of moderate-intensity exercise per week can produce a significant effect on TNF-α, but to produce substantial changes in IL-6, it is required a longer period of intervention at higher intensity.

Although high-intensity exercise demonstrate best results on inflammatory markers when compared with moderate intensity, its application requires caution, because the incident of physical limitations and pathological conditions in the musculoskeletal system is high in this population, and high-intensity exercise can cause negative outcomes by making participants to quit the exercise program.

As limitations we recognize the presence of obesity and postmenopausal state as variables of the study, and both conditions are associated with inflammation. In addition, the absence of direct measurement of VO$_2$peak can be considered a limitation, however, we point out that this study was conducted among patients of health care units of the Brazilian National Health System, facilities that don't have sophisticated laboratory resources. Therefore, we have chosen methodological alternatives that were applicable to their reality, and the Rockport walking test seemed to be a good option.

In summary, the combination of aerobic exercise and resistance training at moderate intensity was effective in reducing inflammation, but some key factors (chronic diseases, previous medical condition, duration, volume and intensity of exercise program and modifications in body fat) had a substantial influence on IL-6, TNF-α, and IL-10 levels, and therefore should be taken into consideration in studies and clinical practice involving intervention programs. Thus, the implementation and maintenance of similar exercise programs can contribute to reduce chronic low-inflammation among obese postmenopausal women.

Acknowledgments

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