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The Effects of Eight Weeks of Aerobic Training and Resveratrol Supplementation on Oxidative Stress Markers in Women with Metabolic Syndrome

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A B S T R A C T

Background: The aim of the present study was to investigate the effects of eight weeks of aerobic training and resveratrol supplementation on oxidative stress markers in women with metabolic syndrome.
Methods: In a double-blind study, 32 overweight women with metabolic syndrome were randomly categorized into four groups of aerobic exercise, resveratrol supplement, exercise plus the supplement, and control. The exercise protocol was eight weeks long with three 60-min sessions every week. The supplement and placebo dose was 400 mg/day. Serum malondialdehyde and total antioxidant capacity were measured at the beginning and end of the study.
Results: Eight weeks of aerobic exercise led to a significant decrease in malondialdehyde and a significant increase in total antioxidant capacity in the exercise, exercise plus supplement, and resveratrol supplement groups compared with the control group, with the greatest effect being observed in the exercise plus supplement group.
Conclusion: Using resveratrol along with aerobic exercises can be effective in attenuating oxidative stress. Further studies with larger sample size are needed to confirm these results.

Introduction

Metabolic syndrome is a multifactor metabolic disease with no definite treatment. In general, the disease is more prevalent in women in Iran and in the world [1]. Its prevalence depends on gender, age, race, social habits, environmental factors, lifestyle, lack of physical activity, and exposure to environmental risk factors [2]. The number of individuals with this disease is growing in Iran and some other countries [3].

There are several factors known to be involved in the pathogenesis of metabolic syndrome, including obesity, inflammation, lipid metabolism disorders, and oxidative stress [4]. The mutual effects of these factors also play a key pathological role [5]. Oxidative stress is caused by an increase in reactive oxygen species (ROS) or a decrease in antioxidant enzymes such as catalase, superoxide dismutase, and glutathione peroxidase. Malondialdehyde (MDA), protein carbonyl content (PC), total antioxidant capacity (TAC), and ROS are the potential biomarkers of oxidative stress [6].

Oxidative stress decreases aerobic capacity and interrupts skeletal muscle energy metabolism in patients with metabolic syndrome [7]. In fact, the mechanical and metabolic stresses caused by vigorous exercises might trigger oxidative stress and inflammatory responses [8], which in turn decreases physiological capacity and increases biomolecular damage markers including MDA, PC, and 8-OHdG [9]. The level of oxidative stress in individuals with metabolic syndrome is high, resulting in attenuation of the aerobic capacity [10-11]. Considering the positive effects of exercise training on oxidative stress, on the one hand, and the antioxidative effects of resveratrol, on the other hand, it seems reasonable that a combination of aerobic training and resveratrol supplementation would lead to a synergistic effect on the attenuation of oxidative stress and an increase in antioxidant capacity. Taking into account the paucity of studies on the effects of

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resveratrol on MDA and TAC in patients with metabolic syndrome and the combined effects of resveratrol and aerobic exercise on oxidative stress in the patients, the present study was aimed at examining the effects of eight weeks of aerobic training along with resveratrol supplementation on oxidative stress in women with metabolic syndrome.

Subjects and methods

Study design

This was a double-blind study with pretest-posttest design and a control group. After securing the required permissions form the Islamic Azad University, East Tehran Branch (ethics committee ID: IR.IAUETB.61009), the participants were selected. Inclusion criteria were being ≥18 years old, having a BMI of ≥18.5 kg/m^2, not using any specific medicine, having no chronic disease, having at least 3 out of the 5 symptoms of metabolic syndrome, and not participating in any exercise program. The exclusion criteria were failing to attend more than three exercise sessions, no deformity, and reluctance to participate. The participants attended Mokhaberat Sports Facilities and were briefed about the study, its objectives, the exercise protocol, the supplementation, and the possible risks.

A personal information questionnaire and an informed consent form were filled out by the participants, and anthropometric and blood pressure indices were measured for all the participants. The participants' Vo_{2max} was assessed using the Bruce test and the scores were logged as pretest score. After ensuring a random distribution of all the participants and before initiating the training protocol, maximum heart rate (HR_{max}) of the participants was measured and logged ($HR_{max} = age - 220$). Then, the exercise groups underwent the eight-week training protocol. The researcher would check the implementation process, physical condition of the participants, and use of the supplement over the eight-week period. To this end, the researcher would telephone the participants 24 h after each session to check their physical, mental, and mood condition.

Sampling method

Thirty-two patients (mean age: 40.1 years, BMI: 25-29.9 kg/m2) with metabolic syndrome were randomized to one of the four groups of aerobic exercise (n = 8), resveratrol supplement (n = 8), exercise + supplement (n = 8), and control (n = 8).

Exercise protocol

The aerobic exercise groups performed 60-min aerobic exercise 3 days per week for eight weeks. The exercise protocol consisted of 5-10 min of warm-up and stretching exercises, 40-50 min of treadmill running at 60% to75% HR_{max}, and 5-10 min of cool-down and stretching exercises [12].

Supplement

Aerobic exercise group plus resveratrol supplement followed the same exercise protocol along with fasting intake of resveratrol supplement at 400 mg/d (Barij Essence Pharmaceutical Co., Kashan, Iran) [13]. The resveratrol supplement group only took resveratrol supplement throughout the study and had no exercising. The control group continued with their daily activities, which did not include exercise or using supplements.

Biochemical measurement

The participants appeared in a laboratory 24 h before initiation of the intervention, and fasting blood samples were taken from the brachiocephalic vein. Postintervention blood samples were taken 48 h after the last exercise session—to make sure that inflammatory effects of the exercise on physical condition of the participants are minimized.

Statistical analyses

Data analyses were carried out on SPSS V. 23. The Kolmogorov-Smirnov test was used to examine the normality of the data distribution. No outlier value was detected among the data. The quantitative variables were expressed as mean ± standard deviation (SD) and qualitative variables were described as frequency. To ensure random distribution of the data, we compared the groups on baseline characteristics using a one-way ANOVA. The results indicated no significant difference, which meant that the participants were grouped randomly. An ANCOVA test was used to remove the effects of confounding variables. Moreover, the Bonferroni post hoc test was used to compare the groups pairwise. It is notable that the study was carried out as a double-blind work, and data were analyzed using the intention-to-treat approach. Instead of the data of the individuals who were excluded (n = 2), the baseline data were used [14-16]. Analyses were performed with significance level set at $\alpha = 0.05$.

Results

Participant characteristics

Totally, 32 individuals took part in the study.

Baseline characteristics of the participants are summarized in (Table 1). There was no significant difference among the four groups in height, weight, or BMI. Moreover, two participants were excluded for failure to attend the pretest stage (one in supplement and one in the control group).

Table 1. Characteristics of the participants

Characteristics	Resveratrol group (n = 8)	Exercise group (n = 8)	Resveratrol + Exercise group (n = 8)	Control group (n = 8)	P value[a]
Age, y	39.8 ± 1.3	40.5 ± 1.7	39 ± 1.5	41.2 ± 2.3	0.89
Height, cm	162 ± 3	159 ± 2	160 ± 4	163 ± 4	0.94
Weight, kg	71.1 ± 2.1	72.3 ± 1.3	70.2 ± 1.6	74.3 ± 1.8	0.96
BMI, kg/m2	27.1 ± 2.1	28.6 ± 2.1	27.4 ± 2.1	28 ± 2.1	0.91

BMI: body mass index
All values are expressed as means ± SD
[a]ANOVA

Serum MDA levels

There was a significant decrease in serum MDA levels in the supplement and supplement plus exercise groups after the intervention. These differences remained significant even after adjusting for baseline levels using an ANCOVA test (p = 0.001).

Given the adjusted mean ± SD, the exercise and exercise plus supplement groups had lower mean values compared with the other two groups (Table 2).

Table 2. Serum MDA levels in the participants

		Resveratrol group (n=8)	Exercise group (n=8)	Resveratrol + Exercise group (n=8)	Control group (n=8)	P value[b]	P value[c]
Serum MDA levels, pg/dl	Before	5.1 ± 0.4	5.2 ± 0.7	5.4 ± 0.5	5.1 ± 0.3	0.88	
	After	3.8 ± 0.5	4.5 ± 0.4	3.8 ± 0.8	5.2 ± 0.5	0.001	0.001
	Difference	-1.3 ± 0.2	-0.7 ± 0.3	-1.6 ± 0.6	0.1 ± 0.4	0.001	
	P valuea	0.001	0.12	0.001	0.99		

Data are reported as means ± SD
aTwo related sample tests (Wilcoxon)
bKruskal-Wallis test
cANCOVA

The results of the Bonferroni post hoc test showed a significant difference between the exercise and the supplement groups (p = 0.032) as well as the exercise and control groups (p = 0.001).

Moreover, there was a significant difference between the supplement and control groups (p = 0.041). Other results showed that there was a significant difference between the exercise plus supplement and control groups (p = 0.001) and between the exercise plus supplement and supplement groups (p = 0.012).

TAC serum level

In comparison with the baseline, there was a significant increase in the mean serum TAC level in the exercise, supplement, and exercise plus supplement groups. The difference among the four groups after controlling for the baseline data by the ANCOVA test was significant (p = 0.001). The aerobic exercise plus supplement group had the highest increase in serum TAC among the three groups. To examine the differences, the Bonferroni post hoc test was used (Table 3).

Table 3. Serum TAC levels in the participants of the four groups

		Resveratrol group (n = 8)	Exercise group (n = 8)	Resveratrol + Exercise group (n = 8)	Control group (n = 8)	P value[b]	P value[c]
Serum TAC levels, pg/dl	Before	678 ± 15	665 ± 19	664 ± 16	645 ± 12	0.59	
	After	752 ± 21	724 ± 17	768 ± 15	650 ± 20	0.03	0.001
	Difference	74 ± 18	59 ± 15	104 ± 13	5 ± 16	0.001	
	P value a	0.009	0.012	0.001	0.56		

Data are reported as means ± SD
[a]Two related sample tests (Wilcoxon)
[b]Kruskal-Wallis test
[c]ANCOVA

As showed in Table 3, there was a significant difference between the exercise and supplement groups ($p = 0.047$) and the exercise and control groups ($p = 0.001$) after the intervention. There was also a significant difference between the supplement and control groups ($p = 0.026$). Moreover, there was a significant difference between the exercise plus supplement and control groups ($p = 0.001$) and between the exercise plus supplement and supplement groups ($p = 0.001$).

Discussion

The present study showed that eight weeks of aerobic exercise along with resveratrol supplement led to a significant decrease in serum MDA levels. At a low physiological level, ROS function as redox messenger (oxidation and reduction) in intracellular signaling and regulation [17]. In a perfect condition, there is a balance between antioxidant defense system and ROS. Oxidative damage happens when the balance between the level of antioxidants and radicals is disrupted and the level of free radicals increases [18-19]. In the case of prolonged oxidative stress, the vital biomolecules (e.g., DNA) might be damaged, leading to biological consequences, including disruptions in signaling pathways and gene expression, mutation, transformation, and apoptosis. MDA is an oxidant and free radical subclass and also altered form of peroxide hydrogen (H_2O_2). In general, DNA and membrane of the cell are the most damaged parts by the free radicals and MDA. The findings of this study are consistent with those of Farzanegi et al [20], Xiao [21], Mathieu et al. [22], and Farinha et al. [23]. In contrast, Rahbar and Ahmadi Asl [24] reported that three months of weight-lifting training made no significant changes in MDA in rats. This inconsistency could be due to the differences in training mode (resistance vs aerobic exercise) and in the participants (animal vs human). It merits mention that aerobic exercises are not the only way to generate free radical; intense and heavy physical exercises also generate free radicals in the skeletal muscles and other body tissues [25].

Our study also showed that eight weeks of aerobic training along with resveratrol supplement led to a significant increase in TOC. The increase in TOC in the aerobic exercise plus supplement, supplement, and aerobic exercise groups compared with the control group indicates the important role of using supplement along with exercise in improving the antioxidant systems of the body to maintain hemostasis of tissues and cells. Following an increase in oxidative stress in the body, cellular defense mechanisms, including antioxidant enzymes, are activated to fight the oxidative stress [26-27]. Aerobic physical activities increase secretion of hormones such as catecholamines, which lead to an increase in oxidative stress and lipid peroxidation [28]. On the other hand, a decrease in tissue blood flow happens at the initiation of exercise as the blood is supplied to active muscles, kidneys, spline, and liver followed by re-establishment of tissue blood flow as the exercise goes on. This is another factor effective in the increase of lipid peroxidation [25].

The results of this study are consistent with Saberi et al. [29], Chevion et al. [25], and Gharakhanlo et al. [30] and inconsistent with Venojärvi et al. [31] and Bo et al. [32], who demonstrated that aerobic exercises without supplement had no effect on antioxidant capacity. The inconsistency between the present study and other studies is expectable given that excessive oxygen supply to tissues is one of the causes of increased oxidative stress and that the exercise-induced oxidative stress is affected by factors such as health condition, age, gender, genetics, physical fitness, individual differences, different tissue responses, muscle fiber type, exercise intensity, and nutritional status [21]. More importantly, the diversity of lipid peroxidation indices and measurement methods with different sensitivity further explain the inconsistency in the findings.

Conclusion

In conclusion, aerobic exercise with or without resveratrol supplement can be effective in improving oxidative stress indices in patients with metabolic syndrome. Therefore, the findings can be interesting to medical, exercise, and nutrition professionals. Moreover, patients with metabolic syndrome are recommended to do exercise and use antioxidant supplements.

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Abbreviations

BMI: Body mass index; MDA: Malondialdehyde; HRmax: Maximum heart rate; PC: Protein content; ROS: Reactive oxygen species; TAC: Total antioxidant capacity.

Disclosure statement

There are no competing financial interests.

Author contribution

The present study was done as the master's thesis of SH under the supervision of AD.

Conflict of interest

None of authors have conflict of interests.

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