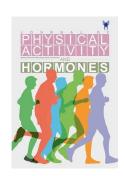


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The effect of combined aerobic-resistance training on plasma estrogen and progesterone and its relationship with lipid profile in Menopausal women

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Abstract

Introduction: This study aimed to determine the effect of eight weeks of combined aerobic resistance training on estrogen and progesterone levels and their relationship with serum lipid profiles in menopausal women.

Material & Methods: This study was conducted on 22 menopausal females aged between 49-65 years who volunteered to participate (weight, 64 -102 kg; height, 150-165 cm). They were randomly divided into the exercise group (EG=12) and the control group (CG=10). The EG performed aerobic-resistance exercises for 90 min, 3 d /week for eight weeks. Height and weight, waist circumference (WC), body mass index (BMI), body fat percentage (Fat %), aerobic and anaerobic capacity, lipid profiles, Serum estradiol and Progesterone hormone were measured before and after 8 weeks of exercise training. The data analysis was done with SPSS version 24 and a significant level of P≤0.05 was considered.

Results: The results showed that compared to the pre-test, in the post-test, EG had significantly reduced weight, WHR, BMI, Fat%, and an increase in Vo2max and estradiol; however, CG showed a decrease in HDL and Vo2max (P < 0.05). Also, in the inter-group comparison, this exercise training significantly promoted the EG group's anaerobic and aerobic power (P < 0.05).

Conclusion: Finally, The results showed that the combined training that consists of endurance and resistance training in eight weeks can improve body composition in postmenopausal females. Similarly, this exercise increased aerobic capacity and estradiol in menopausal women. The results indicated that combined exercise can keep serum lipids in their normal range.

1. Introduction

Menopause is a gradual natural process in females aged 42-55 and is defined as the "cessation of the menstrual period" (1). The rate of postmenopausal in developed and developing countries is 15 percent and around 5-8 percent respectively. However, this rate is expected to rocket up and reach 1.2 billion females by 2030. Menopause has a significant effect on physical and mental health. It is

necessary to identify factors associated with late and early menopause because of their effects (2). For instance, many studies have shown that age in menopause is a significant factor for onsetting specific chronic diseases such as cardiovascular diseases, breast and endometrial cancer and osteoporosis and at high risk for bone fractures (3). estrogen and progesterone play a vital role in female physiology and may be modulated by exercise(4). Sex steroid receptors are present in virtually all anatomic systems. There is a complex relationship between the impact of aging,

behavioral/environmental risk factors, and the impact of menopause sex steroid depletion on the presence and course of chronic disease (5). Around 80 percent of females experience symptoms such as hot flashes, night sweats, insomnia, tiredness and fatigue, concentration impairment, low mood, anxiety, mood swings, irritability, and loss of confidence due to the reduction in sexual hormones including testosterone and estrogen (6). For instance, studies showed that prolonged decreases in estrogen increase the risk of cardiovascular disease and osteoporosis (7). Also, another study showed that estrogen reduction plays a crucial role in the development of metabolic syndrome after menopause transition (8). Studies showed that females with problematic menopause reported low levels of health-related quality and as a result, they use healthcare services far more than females without problematic menopause. Physical activity is a beneficial way to reduce the unexpected symptoms of menopause, and there is significant evidence to show that it is playing a protective and supportive role against chronic problems in terms of coronary heart disease, obesity, diabetes, and mental health problems in the long term (9).

Exercise is one of the physical activities that is well structured, planned, and repetitive to improve and maintain physical fitness (10). Combined exercises that are performed in the form of different types of sports exercises (for example, aerobic resistance exercises) during a training session or with a difference of several hours in a day, can affect the biological processes of the body (11) .Physical activity has shown its efficacy in metabolic disturbances. Menopausal females with good physical activity showed a lower BMI (less fat mass but more lean mass). Furthermore, reports of menopausal females showed the impacts of menopause transition on the frequency and tendency of physical activity. It decreases the frequency of physical activity, though increases the tendency for activeness and this desire is propagated when it is recommended by a health professional. Getting medical help from a GP to reduce menopausal side effects is ordinary but not widespread because of the difficulties in access to medical settings in different regions. Menopause symptom management includes strengthening evidence-based for all intervention options (12). A Studies suggested different ways to decrease menopause symptoms such as medication and physical activity. The latter seems to be a good choice because it has a positive effect on muscle volume and bone density which can lead to better body movement and balance of muscle coordination, so, there would be a lower risk of falling (13). Resistance exercise enhances muscle hypertrophy by increasing muscle protein synthesis and increasing the cross-section of fast muscle fibres, and on the other hand, aerobic exercise increases mitochondrial ATP production in skeletal muscles and also increases muscle protein synthesis. In general, it improves exercise performance by increasing aerobic metabolic capacity and increasing cardiovascular and respiratory endurance (14). A study showed that progressive strength exercise has a positive effect on physical ability and lean volume which can expanded to the menopause stage (1).

In general, various researches related to the effects of exercise on estrogen, progesterone, and blood lipid profile, as well as blood pressure and heart rate of postmenopausal females, have been done, which showed different results. For example, some researchers found a positive effect of aerobic exercise on estrogen, progesterone, serum lipid, blood

pressure, and heart rate (15-18), but others did not show these effects (19, 20). Despite the recognized importance of sex hormones, studies provide a mixed understanding of how physical activity specifically affects these hormones. Studies have investigated the effects of distinct types of methods, intensity, and duration of exercise on the levels of sex hormones in females. However, these studies show different methodological diversity and contradictory findings. Therefore, they pose challenges for generalizable conclusions (4). There are several systematic reviews and meta-analyses in the literature that examine the effect of exercise training on VO2 max. However, little is known about the overlap of primary studies included in these systematic reviews and/or meta-analyses (21). Based on this evidence it is clear that given active therapeutic exercise has various advantages for different conditions. This study aims to determine the effect of combined (aerobic resistance) training on plasma female sexual hormones and its relation with serum lipids in menopausal females.

2. Methodology

2.1. Materials and methods

This study was quasi-experimental research conducted in a clinical trial.

2.2. Participants

In this study, the sample consisted of 26 eligible postmenopausal females (54.83±4.72 years) who were volunteers to participate in this research. The inclusion criteria were: average time after menopause was 1 year, no medication use, and no history of exercise training at least six months. Samples were randomly divided into experimental (EG) and control groups (CG). Three participated in CG and one from EG were excluded from the study.

2.3. Measurements

Body composition measurement: Height and weight were measured in light clothing without shoes. Waist circumference (WC) was measured using a tape measure placed halfway between the lower border of the ribs and the iliac crest in a horizontal plane. Height, weight, and WC were measured twice and the averages were taken. Height, WC, and weight were measured to the nearest 0.1 cm and 0.1 kg, respectively. Body mass index (BMI) was calculated by dividing the participant's weight (kg) by the square of height (m2). Body fat percentage was calculated using the three-point method of Jackson and Pollock. In this method, the skin folds of the triceps, upper arm, and thigh areas on the right side of the body were measured with a caliper (SAEHAN, SH5020, Korea) and entered in the following formula:

% Body Fat = $(0.41563 \times \text{sum of skinfolds}) - (0.00112 \times \text{square of the sum of skinfolds}) + <math>(0.03661 \times \text{age}) + 4.03653$, where the skinfold sites (measured in mm) are abdominal, triceps, and suprailiac (22).

Aerobic capacity: Cardiorespiratory capacity was determined by measuring the maximum oxygen consumption (VO2max). The Rockport one-mile submaximal exercise test, which has been proven to be a reliable and valid protocol in predicting VO2max in untrained participants, was performed. The reliability coefficients of the Rockport test are more than 0.93 and its validity coefficient is more than 0.325[55]. In

addition, the Rockport one-mile submaximal test lessens problems of exhaustion and injuries associated with exercise testing (23). Maximal oxygen uptake scores were predicted from the Rockport one-mile walking test formula: VO2max = $132.853-(0.0769 \times \text{body mass})-(0.3877 \times \text{age})+(6.315 \times \text{gender})-(3.2649 \times \text{time})-(0.1565 \times \text{HR})(24)$. The procedure of the test started with a warm-up of about 8–10 min. The participants' post-exercise HR and times to complete the one-mile distance was recorded using a polar HR monitor (24, 25).

Anaerobic capacity: It was done using the Wingate test. The Wingate test was preceded by a 5-minute warm up with a load of 90 watts on a cycloergometer (Monark E834, Sweden) during which the participant performed (in the second and fifth minute) two maximal accelerations lasting about 5 seconds. After the warm up, there was a 5-minute rest break before the main test. The test had a stationary start34 and lasted 30 seconds, with a load of 7.5% of body mass. In addition, the subjects underwent a 2-3 minute cool-down period at low to moderate levels of aerobic equilibrium (26).

Blood biochemistry: A blood sample was drawn after a 12-hour fasting period. Serum lipid profiles (total cholesterol, triglyceride (TG), cholesterol(C), HDL-C, and blood glucose were measuring the baseline and at the end of 8 weeks. Immunized turbidimetry methods measured LDL-C and HDL-C directly with commercially available kits (Pishtazteb, Tehran, Iran). Serum TG was analysed using a total glycerol test kit, cholesterol was analyzed using a total cholesterol test kit, and Serum glucose was analysed using a total glucose test kit (Biosystems, Barcelona, Spain) by full automation glycerol phosphate oxidase/peroxidase/endpoint methods. All measurements were carried out on a Hitachi747 autoanalyzer (Hitachi Ltd., Tokyo, Japan). All of the variables were measured at the beginning of the trial and week, in both the exercise group and control group, by one of the researchers (25).

Evaluation of serum hormone levels: Serum estradiol hormone is measured with using chemiluminescence method (Biome Rio kit, Vidas, France). Normal values in Postmenopausal are less than 3 pg/ml. Progesterone hormone is measured using the ELISA method (Damtra, Italy). Normal values in postmenopausal are less than 4 ng/ml).

2.4. Intervention

Exercise training program: The training protocol consisted of three sessions/week for 12 weeks. The exercise training program of the experimental group includes training for 90 minutes, consisting of 10 minutes of warm-up, 35 min aerobic training with 50-80% of the maximum heart rate, 35min resistance training with 50-70% of one maximum repetition(1RM).

Progressive aerobic exercise: including 35 minutes of aerobic exercise with an intensity of 50-80% of the maximum heart rate (220 - age) in the final sessions. Aerobic exercises on a treadmill (BC89000, Titan Fitness Industrial Co., LTD., Taipei, Taiwan) were done progressively.

Progressive resistant exercise: The participants perform resistance exercises three times a week for 90 minutes, (including 3 sets, 8 repetitions, 30 seconds rest between each repetition, and two minutes rest between each set). Each resistance training session consisted of 8 exercises that were performed as follows: chess press, stretching, front arm, leg press, front leg, back leg.

In the first and second weeks, the workload for each exercise was equal to 50% of each one repetition maximum (1RM) consisting of 8-10 repetitions per set. The resistance training program started with 60% of 1 repetition maximum and gradually increased to 80% (figure 1.). To obtain a maximum repetition by recording the amount of weight and the number of repetitions in the Brzycki Equation (Weight \div (1.0278 - (0.0278 \times Number of repetitions)), the maximum strength of the subject in each movement Obtained.



Figure 1. Resistance exercise program

2.5. Statistical Methods

In the inferential statistics section, first, the Kolmogorov-Smirnov test for the normal distribution of the data and the test. Independent and paired t- test was used for normal data and Mann-Whitney U and Wilcoxon test for nonnormal data. Statistical analysis was conducted using SPSS software (version 26). The level of significance in all statistical analyses was set at P<0.05.

3. Results

The results of statistical tests for normal and non-normal data are presented in Table 1.

Table 3. The result of comparison between pre and post test,

exprimental group (n=12), control group (n=10)

Variable	Group	Pre-test	Post-test	Intra	inter
		Mean ±SD	Mean ±SD	group	group
				sig	sig
Weight(kg)	CG	71.56±6.90	71.95±7.22	.289a	.509b
	EG	76.33±11.05	74.58±10.44	$.002^{c^*}$	
WHR	CG	.87±.15	.91±.14	.252a	.418 ^d
	EG	.93±.13	.92±.11	$.002^{c*}$	
BMI(kg/m ²)	CG	28.53±2.58	28.67±2.90	.147a	.596 ^b
	EG	30.92±1.11	29.48±3.97	$.002^{c*}$	
Fat%	CG	34.82±3.91	35.13±4.27	.751a	.852b
	EG	37.3±2.27	34.84±2.34	$.001^{a*}$	
Vo2max	CG	16.07±1.7	14.2±1.14	$.005^{c*}$.001d*
ml/kg/min	EG	17.74±2.1	23.09±2.03	$.002^{a^*}$	
Anaerobic	CG	372.82±85.91	361.44±86.12	.92a	$.004^{b*}$
power watts	EG	385.33±82.3	399. 5±92.11	$.46^{a}$	
TG mg/dl	CG	191.60±90.31	193.14±87.2	.38c	.28 ^d
	EG	179.08±88.31	168.12±81.24	.43a	
Cholestrol	CG	201.42±30.18	206.8±32.27	.87 ^c	$.17^{b}$
mg/dl	EG	181.31±31.14	188.25±33.1	.43a	
LDL mg/dl	CG	219.16±33.82	227±34.1	$.48^{a}$.63b
	EG	121.83±42.76	136±41.9	$.09^{a}$	
HDL mg/dl	CG	39.3±5.1	37.25±4.36	$.03^{a*}$.62 ^d
	EG	33.17±8.07	37.25±7.29	$.09^{a}$	
Estradiol	CG	17.9±1.8	18.7 ± 2.3	.07 ^c	.87 ^d
pg/ml	EG	18.3±2.1	20.1±1.6	.03c*	
Progestrone	CG	15.7±3.4	14.8±4.3	.52°	.77 ^d
ng/ml	EG	14.9±2.5	15.2 ± 2.2	.108c	

CG, Control Group; EG, Experimental Group; a, t – paired test; b, t independent test; c, Wilcoxon test; d, mann whitney u test)

The results of the above table showed that compared to the pre-test, in the post-test, EG had significantly reduced weight, WHR, BMI, Fat%, and an increase in Vo2max and estradiol; however, CG showed a decrease in HDL and Vo2max. Also, in the inter-group comparison, this exercise training significantly promoted the EG group's anaerobic and aerobic power (Vo2max).

4. Discussion

The present study discussed the effect of a combined training course (resistance aerobics) on estrogen levels and progesterone and its relationship with serum lipids in postmenopausal females. The results of the research showed that a combined training course is effective for postmenopausal females' body composition indicators. In fact, in the EG comparing the data in the pre-test and post-test in percent Fat, body mass index, waist-to-hip ratio, and weight decreased significantly. Several studies have evaluated exercise as a therapeutic intervention, but the type, duration, intensity, and frequency of training varied, and different indicators were evaluated in each study. For example, a study showed that in postmenopausal females, 6 to 7 percent weight loss was achieved mainly by combining endurance and strength training, leading to a more favorable body composition and better physical fitness (27). Shabani showed that weight, BMI, and WHR significantly reduced after 8 weeks of endurance resistance exercise. Also, exercise training decreased plasma levels of hs-CRP, IL-6, and fibrinogen (28). In another study, when training loads were equal, aerobic and combined exercise decreased core fat and increased FFM, but only combined exercise enhanced body fat percentage reduction in obese postmenopausal females after an exercise program(29). Fallah et al. showed that regular walking programs can decrease body composition (Body weights, percent body fat, and body mass index significantly), and increase percent muscle mass, however, it may not be effective in reducing systemic inflammatory markers(30). The inconsistent results of some studies show that there is no difference between the benefits of different exercise programs in weight loss/gain, however, the duration of the exercise (8 weeks) may be needed to measure more changes in weight. A significant difference between the two sample groups in other previous studies with a longer intervention duration (12 weeks)(31) has inconsistency in their results, though they identified different factors for this inconsistency in terms of age, the length of training, and physical condition. Probably, the results of inconsistent studies are different from the results of the present study due to the type of exercises used, which were often short-term resistance or aerobic exercises.

The research results showed that compared to the pretest, there was a significant increase in aerobic power in the EG in the post-test, but there was no significant increase in anaerobic power in both groups. By this finding, the results of McRae et al.'s research show that aerobic exercise is effective in improving total body resistance and muscle endurance, and there is a significant difference in maximum oxygen consumption in the exercise group (32). The results of the Khartomi et al. study were in agreement with the present research result (33). Contrary to the results of our study, Amati et al showed that aerobic exercise with an intensity of 75% of the maximum heart rate does not affect the VO2 max in females (34). in another study, data observed during the aerobic exercise were similar for the degree of change in VO2 max both the control and groups studied (35). en et al. found that the degree of change in VO2max induced by aerobic and resistant training varied by population with greater improvements seen from a healthy nonathletic population, compared to an athletic population(36). It seems that the reason for the difference in results can be attributed to the difference in age, the length of the training period, the physical condition of the subjects, and the duration of the training (33).

Our study showed that eight weeks of supervised aerobic and resistance training had no significant effect on the metabolic marker consisting of LDL, blood sugar, and TG in the CG, and EG and HDL had a significant decrease in the CG. Consistent with this finding, a review study concluded that long-term exercise, except for TG, significantly benefits MetS risk factors, and moderate and combined exercise, except for HDL, significantly reduces Mets risk factors (37). This study was novel in that it investigated the body composition and metabolic profile of postmenopausal females by separating them into positive and negative responders to combined training-induced changes in HDL-c. It was verified that a huge individual heterogeneity in HDL-c changes and the negative responders presented higher baseline values for android-to-gynoid fat mass ratio, while the positive responders showed decreased triacylglycerol and VLDL after training intervention (38). The results of another study showed that the percentage of females with the target concentration of the lipid fraction increased significantly in both exercise groups, and no significant changes were observed in the studied parameters in the control group (15). Shabani et al. found that a period of concurrent endurance and resistance training can decrease BMI, heart rate (HR), systolic and diastolic blood pressure, triglyceride, highsensitivity C-reactive protein (CRP), and promote significantly high-density lipoprotein, and VO2max during the 8 weeks (39). Moreover, no changes were found in the cardiovascular risk factors of women who did not exerciseResearchers believe that HDL and LDL levels are hardly affected by exercise and the mechanism of its changes is complex. Among them, enzymes such as lipoprotein lipase, triglyceride liver lipase, and cholesterol carrier proteins are effective in HDL concentration. In the present study, the amount of LDL in the EG did not increase significantly in the post-test phase compared to the pre-test. Also, in terms of the mechanisms involved in the process of increasing the LDL level, it can be said that performing sports activities will not have much effect on the lipid profile in people with normal TG levels.

Our result of the 8-week randomized control trial study suggests that intervention based on aerobic and anaerobic exercise does improve the level of circulating estrogen in postmenopausal females. But in CG there wasn't have significant difference. Also, progesterone in the control and experimental groups didn't have a significant difference. Some studies have shown conflicting findings regarding the effect of exercise on estrogen and progesterone in postmenopausal females. A study consistent with our findings showed that estrogen levels increased significantly after an exercise program (40). Shabani et al showed body mass index, body fat percentage, heart rate variable, and serum cortisol had decreased; and serum estradiol had increased among overweight and obese postmenopausal women with impaired fasting blood glucose after eight -week combination resistance-aerobic exercise (41). Conversely, Kenny et al.'s study found that several exercise programs ultimately lead to lower estrogen levels (42). Also, in a systematic review, eleven studies were included. In this study, the effect of exercise on oestradiol concentration and progesterone level was not significant (4). Seighali et al. showed No significant difference was observed in follicle-

stimulating hormone, estradiol, dehydroepiandrosterone(43). In another study, researchers did not find significant changes in FBS, LDL-cholesterol, HDL-cholesterol, triglycerides (TG), waist circumference, and blood pressure (44). In general, it seems that the reason for the difference in the findings is that the duration of the exercise sessions varied from one session to four months, and of course, the evaluation methods were using blood or urine samples. The level of sex hormones serves as an objective indicator to evaluate the effectiveness and level of exposure to physical activity. If exercise affects these levels, it can determine the type and dose of physical activity necessary for optimal health. The limitations of this study include the small sample size, and dietary control could affect the research findings.

5. Conclusion

The results of this research showed that the combined training that consists of endurance and resistance training in one session improves body composition in postmenopausal females. Similarly, combined exercise increased aerobic capacity and estradiol in these females. However, although there is no significant difference in the level of serum lipids, the results indicated that combined exercise can keep serum lipids in their normal range.

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Conflict of interests: The researchers declare no conflicts of interest.

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