

The Effect of Combined Training on Estradiol Levels and Metabolic Risk Factors in Overweight and Obese Postmenopausal Women

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Abstract

Objective: Menopause is a normal biological process associated with hormonal and metabolic changes. The purpose of this study was to investigate the effect of combined training on estradiol levels and some metabolic risk factors in obese and overweight postmenopausal women.

Materials and Methods: In this quasi-experimental study, 24 postmenopausal women were randomly divided into experimental and control groups. Subjects of experimental group were performed 10 weeks of combined training including resistance and aerobic exercises. Control group did not participate in any exercise training. Fasting glucose, insulin, estradiol, HOMA-IR and body fat percentage measured at the beginning and after training.

Results: There were no significant differences in estradiol (P -value: 0.87), glucose (P -value: 0.09), insulin (P -value: 0.11), HOMA-IR (P -value: 0.08) and body fat percentage (P -value: 0.24) between experimental and control groups after combined exercise training.

Conclusion: This study showed that 10 weeks of moderate-intensity combined exercise training has no effect on serum estradiol level and insulin resistance in overweight/obese postmenopausal women.

Keywords: Estradiol, Metabolic risk factors, Combined training, Postmenopausal women

Introduction

Menopause is a substantial stage in women's life that is associated with metabolic changes and possibly an increased risk of type 2 diabetes (1). After menopause, adipose tissue is the main source of estrogen biosynthesis through aromatase activity (2). On the other hand, it has been reported that among postmenopausal women

circulating levels of steroid sex hormones, especially estradiol, were positively associated with increased risk of type 2 diabetes (3). Therefore, concentrations of estradiol may play important roles in the pathogenesis of type2 diabetes in postmenopausal women (4). Given that obese postmenopausal women have higher circulating estrogen levels compared to

lean postmenopausal women (5), the relationship between menopause and the risk of type 2 diabetes in obese postmenopausal women may be partly due to increased levels of endogenous estrogens. It has also been suggested that insulin resistance plays a major role in the pathogenesis of type 2 diabetes (6) and is positively associated with circulating estradiol in postmenopausal women (7). Insulin resistance and hyperinsulinemia lead to impaired glucose uptake in the muscle and decreased glycogen synthesis in the liver (8). Hyperinsulinemia also increases the risk of developing type 2 diabetes by inhibiting the synthesis of sex hormone-binding globulin in the liver (9). A cross-sectional study, also suggested that serum fasting insulin and blood glucose concentrations are higher in postmenopausal women than premenopausal women (10).

The inverse relationship between the incidence of type 2 diabetes and physical activity is well known (11,12). It has been reported that those who perform 150 min/week of moderate physical activity have a 26% lower risk of developing type 2 diabetes mellitus than inactive individuals (13). However, the effects of exercise interventions on biomarkers of type 2 diabetes risk in postmenopausal women such as estradiol and insulin levels are not well known. In this regard, previous studies have reported desirable changes (14,15) or no changes (16) in the endogenous estrogens after long-term exercise training. There are also conflicting findings about the effect of exercise training on insulin in postmenopausal women. Some studies have reported that aerobic training causes decreased insulin levels and HOMA-IR in sedentary postmenopausal women (17,18). But another study has found no changes in levels of insulin and insulin sensitivity in healthy and sedentary postmenopausal women after combined aerobic and strength exercise training (19). On the other hand, considering the favorable effects of combined training on various aspects of health, the effects of these types of training have been less studied on type 2

diabetes biomarkers in postmenopausal women. Therefore, due to heterogeneous research findings and the need to investigate different types of exercise training, the purpose of present study was to investigate the effect of a period of combined training for 10 weeks on the estradiol levels and some metabolic risk factors in overweight and obese postmenopausal women.

Materials and Methods

In this quasi-experimental study, twenty four overweight/obese postmenopausal women (body mass index $>25 \text{ kg/m}^2$) were selected through purposive sampling method among the volunteers referring to health center in the Zarandieh city, Iran. The sample size was estimated using the Fleiss's formula as in other similar studies (20,21). The participants did not have any regular exercise training in the past 6 months and their last menstruation was at least one year ago. They did not have cardiovascular, metabolic, orthopedic diseases or other chronic diseases. Moreover, none of the participants were underwent hormone replacement therapy. Informed consent was obtained from all participants before their participation in study. They were then randomly assigned into experimental (n=14) and control (n=10) groups.

Physiological and biochemical variables were measured before and after training program. Height was assessed using a stadiometer (Kaveh, Iran). Body weight and body fat percentage were measured using the body composition analyzer (Omron, Finland). Maximal oxygen uptake (Vo_2max) was estimated using the Rockport Fitness Walking Test (22). Overnight fasting blood samples were taken from the antecubital vein at baseline and 48 hours after the last training session. The blood samples were centrifuged at 2500-3000 rpm for 10 min. The serum was separated and stored at $-70 \text{ }^\circ\text{C}$ for subsequent analysis. Serum estradiol was measured by electrochemiluminescence immunoassay kit (Roche, Germany). Insulin was evaluated by immunoradiometric assay kit (IM3210;

Immunotech, Czech Republic). Glucose level was assessed by glucose oxidase method kit (Pars Azmoon, Iran). Insulin resistance was calculated using the homeostatic model assessment of Insulin Resistance (HOMA-IR) (23).

The experimental group participated in a combined aerobic and resistance training program, four times per week for ten weeks. The aerobic training consisted of 25-45 minutes of walking/running at an intensity of 65-75% of maximal heart rate (MHR), two times per week. The aerobic exercise started with the intensity 65% of MHR for 25 minutes and gradually progressed to 75% of MHR for 45 minutes by the end of the 10th week. Resistance training including chest press, lat pull down, biceps and triceps curls, leg press, and leg extension and flexion were performed at 55-65% of one maximal repetition (1RM), 3 sets of 8-12 repetitions with a 2-3-min rest interval between sets. The resistance training was performed two times per week. A 10 minute warm up and 5 minute cool down was included before and after each training session.

Statistical analysis

Normal distribution of data was evaluated by the Kolmogorov-Smirnov test. Independent T-test was used to test the difference in baseline characteristics between the groups. Pre- and post-training differences of all variable were assessed by paired T-test in each group. The analyses of covariance (ANCOVA) was used to compare changes between experimental and control groups. P values less than 0.05 were considered statistically significant. The statistical analyses were performed using SPSS 18 software.

Ethical considerations

This study was approved by the ethics committee of Islamic Azad University of Karaj and registered in the Iranian Registry of Clinical Trial with registration number of IRCT20170918036257N1.

Results

The baseline characteristics of the participants are presented in Table 1. There were no differences in age, height, weight, body mass index, body fat percentage and vo₂max between the two groups (*P*-value > 0.05).

The ANCOVA test showed that there were no significant differences in estradiol (*P*-value: 0.87), glucose (*P*-value: 0.09), insulin (*P*-value: 0.11), HOMA-IR (*P*-value: 0.08), body mass index (*P*-value: 0.12) and body fat percentage (*P*-value: 0.24) between experimental and control groups after combined exercise training. Paired T-test also showed no significant differences between pre- and post-training of these variables in each group. In other words, ten weeks of combined training intervention had no significant effects on measured variables. The values of measured variables in the pre- and post-training are presented in Table 2.

Discussion

In the present study, the effect of 10 weeks of combined training was investigated on circulating estradiol and some metabolic risk factors in overweight and obese postmenopausal women. The results showed that combined training had no effect on the levels of estradiol. Similar to this study, Yoon et al. (2018)

Table 1. Physical characteristics in the two groups (means ±SD)

Variables	Experimental group	Control group	<i>P</i> -value
Age (years)	54 (±2.6)	55.5 (±4.9)	0.37
Height (cm)	154.1 (±2.8)	153.2 (±4.9)	0.59
Weight (kg)	73.4 (±11.7)	75.1 (±9.3)	0.72
Body mass index(kg/m ²)	30.9 (±4.9)	32.1 (±4.6)	0.58
Body fat (%)	43.4 (±6.1)	43.4 (±5.9)	0.98
Vo ₂ max (ml/kg/min)	22.6 (±5.6)	19.1 (±6.4)	0.17

Table 2. Physiological and biochemical variables in pre and post training

Variable	Experimental group		<i>P</i> -value (Within- group)	Control group		<i>P</i> -value (Within- group)	<i>P</i> -value (Between- group)
	Pre-training	Post-training		Pre-training	Post-training		
BMI (kg/m²)	30.9 (±4.9)	30.9 (±4.4)	0.97	32.07(±4.6)	31.03 (±3.3)	0.09	0.12
Body fat (%)	43.4 (±6.1)	43.3 (±6.1)	0.98	43.4 (±5.9)	46.1 (±5.7)	0.12	0.24
Estradiol (pg/ml)	13.9 (±3.2)	15.6 (±4.9)	0.37	15.3 (±3.6)	15.5 (±5.8)	0.94	0.87
Glucose(mg/dl)	85.3 (±16.7)	87 (±11.7)	0.77	82.9 (±11.5)	78.9 (±9.5)	0.44	0.09
Insulin (µIU/ml)	5.03 (±1.4)	5.4 (±1.1)	0.31	5.7 (±1.4)	5 (±0.6)	0.12	0.11
HOMA-IR	1.07 (±0.4)	1.16 (±0.4)	0.33	1.18 (±0.5)	0.97 (±0.12)	0.19	0.08

Also found no significant change in the estrogen level among obese postmenopausal women following 12 weeks of aerobic or resistance training (16). In contrast to our findings, Friedenreiche et al. (2010) showed that 1-year of moderate-to-vigorous intensity aerobic exercise (5d/wk) caused changes in estradiol levels among sedentary postmenopausal women (14). In the another study by Friedenreiche et al. (2015), serum levels of total and free estradiol decreased in inactive postmenopausal women after 12-month of moderate (150 min/week) or High (300 min/week) volumes of aerobic exercise training (15). These contradictions seem to be due to differences in type, intensity, duration, and volume of exercise training that may affect the changes in estradiol. Thus, in the present study, the intensity or duration of combined training may have not been adequate to make favorable changes in serum estradiol levels. On the other hand, it has been suggested that the effects of exercise training on estradiol levels are mediated by a decrease in body fat tissue (24). In this regard, Van Gemert et al. (2015) reported that exercise-induced weight loss led to desirable changes in levels of estradiol among postmenopausal women (25). Also, other studies have shown that weight loss reduces estrogens levels in postmenopausal women (26,27). In one of these, Campbell et al. (2012) found that greater weight loss created greater reductions on estrogens levels in overweight and obese postmenopausal women (27). Therefore, it is possible that physical activity without weight loss does not decrease estradiol levels. The combined training used in our study had no effects on body fat percentage and body mass index, probably due to the diet or short term of

training intervention. In the present study, the participants with no dietary intervention performed the exercise training for 10 weeks, while it has been reported that the combination of exercise and diet compared to exercise or diet alone, have a greater effect on weight and body fat percentage in postmenopausal women (28).

Moreover, in the present study, we found no significant effects of combined training on glucose, insulin and insulin resistance in overweight and obese postmenopausal women. Similarly, Van Gemert et al. (2015) reported that 1-year combined aerobic and strength training has no beneficial effect on the glucose, insulin and insulin sensitivity in healthy and sedentary postmenopausal women (19). In contrast, some studies have reported a decrease in insulin and insulin resistance after aerobic exercise training in postmenopausal women (17,18). It is possible that the intensity or duration of combined training used in the present study have not been adequate to affect insulin and insulin resistance since some studies have shown that intensity (29) and duration (30) of exercise training are important factors for improvement of insulin sensitivity. As Izadi et al. (2018) showed that high intensity interval exercise training compared with moderate continuous exercise training is more effective on insulin resistance in elderly patients with type2 diabetes (31). In another study, Houmard et al. (2004) reported that the duration of exercise should be considered as an important factor in improving insulin action in obese/overweight postmenopausal women (30). On the other hand, some other studies have suggested that the influence of exercise training on insulin levels is modulated through changes in body weight or body fat mass in

postmenopausal women (19,32). For instance, Van Gemert et al. (2015) concluded that exercise may affect insulin sensitivity by weight loss (19). Given these findings, the lack of change in insulin resistance in the present study may be due to inadequate weight or body fat mass changes.

Conclusions

In conclusion, the findings of this study suggested that 10 weeks of moderate-intensity combined exercise training has no beneficial effects on serum estradiol level and metabolic risk factors in sedentary overweight/obese postmenopausal women. It appears that the levels of estradiol and insulin make no favorable changes in response to exercise

intervention that does not reduce body fat mass.

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Conflict of Interest

Authors declare that they have no competing interests.

References

- Slopien R, Wender-Ozegowska E, Rogowicz-Frontczak A, Meczekalski B, Zozulinska-Ziolkiewicz D, Jaremek JD, et al. Menopause and diabetes: EMAS clinical guide. *Maturitas*. 2018;117:6-10.
- Kinoshita T, Honma S, Shibata Y, Yamashita K, Watanabe Y, Maekubo H, et al. An innovative LC-MS/MS-based method for determining CYP 17 and CYP 19 activity in the adipose tissue of pre- and postmenopausal and ovariectomized women using ¹³C-labeled steroid substrates. *Journal of Clinical Endocrinology and Metabolism*. 2014;99(4):1339-47.
- Muka T, Nano J, Jaspers L, Meun C, Bramer WM, Hofman A, et al. Associations of Steroid Sex Hormones and Sex Hormone-Binding Globulin With the Risk of Type 2 Diabetes in Women: A Population-Based Cohort Study and Meta-analysis. *Diabetes*. 2017;66(3):577-86.
- Mauvais-Jarvis F. Is Estradiol a Biomarker of Type 2 Diabetes Risk in Postmenopausal Women?. *Diabetes*. 2017;66(3):568-70.
- Key TJ, Appleby PN, Reeves GK, Roddam AW, Helzlsouer KJ, Alberg AJ, et al. Circulating sex hormones and breast cancer risk factors in postmenopausal women: reanalysis of 13 studies. *Br J Cancer*. 2011;105(5):709-22.
- Baynes HW. Classification, Pathophysiology, Diagnosis and Management of Diabetes Mellitus. *Journal of Diabetes and Metabolism*. 2015;6:541.
- Marchand GB, Carreau AM, Weisnagel SJ, Bergeron J, Labrie F, Lemieux S, et al. Increased body fat mass explains the positive association between circulating estradiol and insulin resistance in postmenopausal women. *American journal of physiology. Endocrinology and metabolism*. 2018;314(5):E448-E456.
- Samuel VT, Shulman GL. The pathogenesis of insulin resistance: integrating signaling pathways and substrate flux. *The Journal of Clinical Investigation*. 2016;126(1):12-22.
- Pasquali R. Sex hormones and the development of type 2 diabetes in women. *Journal of Laboratory and Precision Medicine*. 2017;2:15.
- Yeasmin N, Akther QS, Hasan M, Rabbani R, Rabbani R, Afroz R. Correlation of Estrogen with Serum Insulin and Blood Glucose Levels in Postmenopausal Women. *Bangladesh medical journal*. 2017;46(1):32-7.
- Joseph JJ, Echouffo-Tcheugui JB, Golden SH, Chen H, Jenny NS, Carnethon MR, et al. Physical activity, sedentary behaviors and the incidence of type 2 diabetes mellitus: the Multi-Ethnic Study of Atherosclerosis (MESA). *BMJ Open Diabetes Research and Care*. 2016;4(1):e000185.
- Aune D, Norat T, Leitzmann M, Tonstad S, Vatten LJ. Physical activity and the risk of type 2 diabetes: a systematic review and dose-response meta-analysis. *European journal of epidemiology*. 2015;30(7):529-42.
- Smith AD, Crippa A, Woodcock J, Brage S. Physical activity and incident type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of prospective cohort studies. *Diabetologia*. 2016;59(12):2527-45.
- Friedenreich CM, Woolcott CG, McTiernan A, Ballard-Barbash R, Brant RF, Stanczyk FZ, et al. Alberta Physical Activity and Breast Cancer Prevention Trial: sex hormone changes in a year-

- long exercise intervention among postmenopausal women. *J Clin Oncol*. 2010;28(9):1458-66.
15. Friedenreich CM, Neilson HK, Wang Q, Stanczyk FZ, Yasui Y, Duha A, et al. Effects of exercise dose on endogenous estrogens in postmenopausal women: a randomized trial. *Endocrine-Related Cancer*. 2015;22(5):863-76.
 16. Yoon JR, Ha GC, Ko KJ, Kang SJ. Effects of exercise type on estrogen, tumor markers, immune function, antioxidant function, and physical fitness in postmenopausal obese women. *Journal of Exercise Rehabilitation*. 2018;14(6):1032-40.
 17. Tavallali M, Nouri R, Moghadasi M, Khademosharie M. The effect of eight weeks of walking on blood plasma insulin resistance and protein carbonyl in sedentary postmenopausal women. *Razi Journal of Medical Sciences*. 2019;26(6):64-72.
 18. Friedenreich CM, Neilson HK, Wang Q, Stanczyk FZ, Yasui Y, Brenner DR, et al. Exercise Dose Effects on Insulin Resistance Indicators in Postmenopausal Women: A Randomized Trial. *Journal of Endocrinology and Metabolism*. 2016;6(2):35-45.
 19. Van Gemert WA, Monninkhof EM, May AM, Peeters PH, Schuit AJ. Effect of Exercise on Insulin Sensitivity in Healthy Postmenopausal Women: The SHAPE Study. *Cancer Epidemiol Biomarkers Prev*. 2015; 24(1):81-7.
 20. Fathi M, Attarzadeh Hosseini S, khair abadi S, Hejazi K. Effect of eight Weeks Aerobic Training on Serum parathormone, estrogen and Alkaline phosphatase concentration in obese women with premature menopause. *The Iranian Journal of Obstetrics, Gynecology and Infertility*. 2017;20(7):8-17.
 21. Esmaeili M, Bijeh N, Ghahremani Moghadam M. Effect of combined aerobic and resistance training on aerobic fitness, strength, beta-endorphin, blood glucose level, and insulin resistance in women with type II diabetes mellitus. *The Iranian Journal of Obstetrics, Gynecology and Infertility*. 2018;21(6):34-6.
 22. Kim K, Lee HY, Lee DY, Nam CW. Changes in cardiopulmonary function in normal adults after the Rockport 1 mile walking test: a preliminary study. *Journal of physical therapy science*. 2015;27(8):2559-61.
 23. Fonseca EJNC, Rocha TPO, Nogueira IAL, Melo JB, Silva BL, Lopes EJ, et al. Metabolic Syndrome and Insulin Resistance by HOMA-IR in Menopause. *International Journal of Cardiovascular Sciences*. 2018;31(3)201-8.
 24. Friedenreich CM, Neilson HK, Woolcott CG, Wang Q, Yasui Y, Brant RF, et al. Mediators and moderators of the effects of a year-long exercise intervention on endogenous sex hormones in postmenopausal women. *Cancer Causes Control*. 2011;22(10):1365-73.
 25. Van Gemert WA, Schuit AJ, Van der Palen J, May AM, Iestra JA, Wittink H, et al. Effect of weight loss, with or without exercise, on body composition and sex hormones in postmenopausal women: the SHAPE-2 trial. *Breast Cancer Research*. 2015;2;17:120.
 26. de Roon M, May AM, McTiernan A, Scholten RJPM, Peeters PHM, Friedenreich CM, Monninkhof EM. Effect of exercise and/or reduced calorie dietary interventions on breast cancer-related endogenous sex hormones in healthy postmenopausal women. *Breast Cancer Res*. 2018; 20(1):81.
 27. Campbell KL, Foster-Schubert KE, Alfano CM, Wang CC, Wang CY, Duggan CR, et al. Reduced calorie dietary weight loss, exercise, and sex hormones in postmenopausal women: randomized controlled trial. *Journal of clinical oncology*. 2012;30(19):2314-26.
 28. Foster-Schubert KE, Alfano CM, Duggan CR, Xiao L, Campbell KL, Kong A, et al. Effect of diet and exercise, alone or combined, on weight and body composition in overweight-to-obese postmenopausal women. *Obesity (Silver Spring)*. 2012;20(8):1628-38.
 29. Bird SR, Hawley JA. Update on the effects of physical activity on insulin sensitivity in humans. *BMJ open sport & exercise medicine*. 2017;2(1):e000143.
 30. Houmard JA, Tanner CJ, Slentz CA, Duscha BD, McCartney JS, Kraus WE. Effect of the volume and intensity of exercise training on insulin sensitivity. *Journal of applied physiology*. 2004;96(1):101-6.
 31. Izadi MR, Gandomkar Bagheri H, Mohammadyari S, Ghardashi Afousi AR. Investigating the role of intensity of exercise training on plasma apelin concentrations and insulin resistance in elderly patients with type 2 diabetes. *Journal of Shahid Sadoughi University of Medical Sciences*. 2018;26(3):215-26.
 32. Friedenreich CM, Neilson HK, Woolcott CG, McTiernan A, Wang Q, Ballard-Barbash R, et al. Changes in insulin resistance indicators, IGFs, and adipokines in a year-long trial of aerobic exercise in postmenopausal women. *Endocr Relat Cancer* 2011;18(3):357-69.