



RESEARCH PAPER

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Effects of combined selective aerobic moderate intensity exercises and soya intake on 17β -estradiol (biomarker of breast cancer) and obesity of obese postmenopausal women

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Abstract

To investigate the independent and additive effects of selective short aerobic moderate intensity exercise and soya intake on serum 17β -estradiol and obesity in obese postmenopausal women, this quasi-experimental study conducted in 2006 on women of Uremia, Iran. So 56 obese postmenopausal women were selected and randomly divided into four groups of 14 subjects as follow: exercise-soya, exercise, soya, and control group. Pre- and post-protocol blood samples were collected and the rate of 17β -estradiol concentration was measured. Exercise training within the range of 60-70% maximum heart rate (MHR) was performed for 60 minutes, 3 sessions per week. The subjects of soya group and exercise-soya group had a 100 gram soya nut intake daily for 10 weeks. After The training course, blood samples were taken from the subjects. The collected data was analyzed using Two-way ANOVA and paired t-test. Having soya along with exercise had significant impact on reduction of 17β -estradiol means ($p < 0.05$). Body mass index, waist to hip ratio and weight decreased significantly in exercise-soya group after 10 weeks ($p < 0.05$). Based on the findings of this study, aerobic moderate intensity exercise along with soya intake, decrease obesity and serum 17β -estradiol in obese postmenopausal women.

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Introduction

Menopause is a stage of life that in this period, risk of breast cancer increases (Haghighian *et al.*, 2004). Combination of hormonal, genetic factors and environmental events may play a role in risk of breast cancer (Connolly *et al.*, 2002). The most important risk factor for breast cancer is exposing to estradiol (17 β -estradiol). Estradiol is one of the most important estrogens, which stimulates cell proliferation in breast and endometrium (Anne *et al.*, 2007). High levels of serum estradiol are associated with an increased risk of breast cancer in postmenopausal women (Anne *et al.*, 2007; Timothy, 2003). On the other hand obesity causes increases of serum concentrations of 17 β -estradiol in postmenopausal women because in obese women after menopause, estrogen synthesis takes place mainly in adipose tissue (Timothy, 2003; Anne *et al.*, 2003). Anne MC Tiernan in 505 postmenopausal women with breast cancer, showed that serum 17 β -estradiol, was positively associated with fat percentage and obese women with BMI more than 30 kg/m², had higher serum concentrations of 17 β -estradiol (130%) than women with low weight (22< BMI) (Anne *et al.*, 2003). A meta-analysis that investigated the relationship between body fat distribution and breast cancer incidence rate through waist-to-hip ratio (WHR) reported that the breast cancer rate increased when WHR was elevated to 1.62 (95% CI = 1.28–2.04) as a risk estimate (Connolly *et al.*, 2002). Since, obesity can have the fundamental causes (inheritance) and pathological reasons or is producer of the wrong food habits and sedentary life (Rahmani- Nia and Hojati, 2007), Lifestyle changes such as increasing physical activity and sports programs can be effective in reducing obesity (Timothy, 2003). Regular exercise program with change in BMI and body fat percentage and waist circumference, are associated with hormonal changes (Timothy, 2003; Anne *et al.*, 2003). Several studies have investigated the physical activity on estrogen and estrogen metabolites that are involved in breast cancer. The results of Anne Mac Tiernan (2004) and Pia K. Verkasalo (2001) studies, have

been the role of aerobic exercise in reducing the serum estradiol (Anne Mac Tiernan, 2004; Verkasalo, 2001). However, nutritional factors also affect the level of serum 17 β -estradiol (Lu *et al.*, 2001; Marianne *et al.*, 2008). In this relation, epidemiological studies also have shown that diets containing Soya was associated with reduced risk of breast cancer (Lu *et al.*, 2001). The inverse relationship between breast cancer risks and consuming Soya protein in postmenopausal women was observed in some Asian countries (Marianne *et al.*, 2008). The soybean contains Phytoestrogens genistein, daidzein and glycitein that all these categories are isoflavones and is attached estrogen receptors in breast cells, including 17 β -estradiol receptors (Christine *et al.*, 2007). According to clinical and epidemiological studies, the daily intake of Soya products containing 50 to 200 mg isoflavones may be effective in reducing the risk of breast cancer (Marianne *et al.*, 2008). In this relation, a study on 50 Japanese women indicated an inverse association between Soya intake and serum estradiol concentrations. It has been reported that in Asian women compared with women in Western countries, the concentration of the hormone 17 β -estradiol is about 40 percent less. Probably it is due to the presence of Soya supplements in their daily diets (Mindy, 2002). Considering breast cancer risk also increases in postmenopausal women, and obese postmenopausal women are at risk of breast cancer, Lifestyle changes in order to increase physical activity and improving nutrition would be helpful in reducing obesity and breast cancer risk. Despite the importance and the possible role of physical activity and intake of Soya on serum 17 β -estradiol as an indicator of the risk of breast cancer, research in this area is limited and studies have investigated the effects of prolonged exercise or Soya alone in reducing the risk of breast cancer. The main features of present study was designing of short-term aerobic exercise program with moderate intensity and suitable age and fitness level of postmenopausal women, where to enhance the effectiveness of short-term training program in reducing serum estradiol,

Soya consumption have been helped. Because physical activity and soya may affect hormonal concentrations and energy balance, this study decided to investigate whether short-term aerobic exercise program with moderate intensity is related to the risk of breast?

Materials and methods

The present quasi-experimental pre – posttest was with control group that took as field and laboratory in the city of Urmia.

Subjects

In this study, 56 obese and sedentary postmenopausal women with no during 4 years of no regular exercise and based on original measurements with a $BMI \geq 30$, among the postmenopausal women of Urmia city were selected as a sample, and 49 of them remained till the end of the study. Written and verbal consent was obtained from all participants. Subjects with age: 60.3 ± 5.3 years, menopausal age: 49.6 ± 1.8 years, BMI: 33.91 ± 6.3 kg m, waist to hip ratio: 0.93 ± 0.96 and fat percentage: $29.5\% \pm 4.7$ and a weight of 75.79 ± 15.91 kg. For the older subjects' awareness of their health status, in addition to initial medical examinations, health questionnaires were made.

Participating women were lack of any apparent signs of clinical disease, thyroid, kidney, cardio - vascular and diabetes and did not have history of taking certain drugs (estrogen, progesterone, conjugated - tamoxifen and raloxifene), dietary supplements and drugs. Participants for 2 weeks to assess food intake and physical activity were studied before intervention and then randomly were allocated to one of four groups and blind as a exercise-soya, exercise, soya, and control group. Each group included 14 participants that till the end of the study, three people of exercise - Soya group and 2 people of exercise group were excluded due to lack of regular participation in exercise programs. 2 cases of control group did not attend in the test measurements. At baseline of the study and every two weeks the dietary questionnaire (including a holiday and 2 working days) (Mark *et al.*, 2002) was

used for relative control of subjects feeding, and the physical activity questionnaire (Nancy, 2004) was used to control the level of physical activity levels. BMI (kg/m^2), fat percent were measured by body composition device (Omron), weight (kg) by (seca) made in Germany, the ratio of waist to hip by a special elastic tape graded, and heart rate (beats / min) by the rate meter Polar construction in Finland.

Blood sampling and biochemical measurements

To investigate the biochemical variables, after fasting for 12 hours and one day before the exercise period at 9 am at $25 \pm 3^\circ \text{C}$ at the gym the initial blood sampling was performed. 3 cc of blood from the left hand vein to measure the concentrations of 17β -estradiol subjects using electro chemiluminescence and by Elecsys device product of ROCHE Company with 10 branches of 15 - mol concentration of material was collected. Benefits of electro chemiluminescence method are accuracy and rapid access to the results. After 10 weeks of aerobic exercise with moderate intensity and daily consumption of Soya and After 24 hours of the last session, Collecting blood samples and measurements of other variables in the first phase of the study was conducted.

Program of aerobic exercise with moderate intensity and consumption of soya

Women's Group of exercise - Soya and exercise, participated in three sessions per week, each session lasting 60 minutes (with specified rest intervals) and for 10 weeks of selected aerobic training program, consisting of various movements of aerobics, brisk walking and moderate-intensity running. Exercise intensity based on heart rate in subjects was estimated during an initial pretest consisted of 10 patients using the 60 to 70% heart rate reserve. In the present study, the continuous intensity training through the Polar pulse meters was monitored in said range. Moreover, necessary feedback was given to the subjects in the case of needing to increase or decrease of intensity of exercises. Exercise program with 60 percent

intensity of maximum heart rate (HR max) began in the first and second week and with a gradual increase to 70% (HR max) reached to the ninth and tenth weeks. Women's Group of "exercise - Soya" and "soya" was taking daily 100 grams of soybeans as nuts. In the present study because of easy access to the product of soy nuts in the country and using it easily in sporting facilities and subjects 'workplace, nuts were used for the study of this type of product.

Statistical methods

After testing assuming normal data distribution and equal variance test, Levens test were used for determining the effect of two factors, exercise and soya on the study variables. In the case of being a significant test of variance analysis, LSD post hoc test was used to determine differences between groups. To determine the difference between pre-test post-test, paired t-test was used in each group. Significance level was considered in alpha error level of 5 percent ($p < 0/05$). All the statistical study was performed with spss software of 16th version.

Results

Waist to hip ratio

In this study the effect of Soy and exercise on the distribution of the mean difference of waist to hip ratio was not significant ($P > 0/05$). However, interaction of exercise plus soy was significant on mean difference of this index ($p = 0/046$). Moreover, significant changes of this variable has been under the influence of synergistic effect of exercise + Soy and both intervention of practice + Soya has had additive effect on the mean difference of this variable changes. LSD post hoc tests showed that there is significant difference in mean difference of the distribution between control groups and exercise - Soya groups, Soya and exercise - Soya groups ($p = 0/05$) (Figure 1: a).

Body mass index

Results of variance analysis showed that exercises effect ($p = 0/021$) and interaction of exercises + soy ($p = 0/014$) is significant on the distribution of body mass index mean difference. It seems that a

significant change of this variable has been under the influence of exercise and synergistic effect of exercise plus Soya (Figure 1: b).

LSD post hoc tests showed that there is significant difference in mean difference of the distribution between control groups and exercise - Soya groups ($p = 0/05$). The maximum degree of reduction of this index was related to exercise - Soya group.

Weight

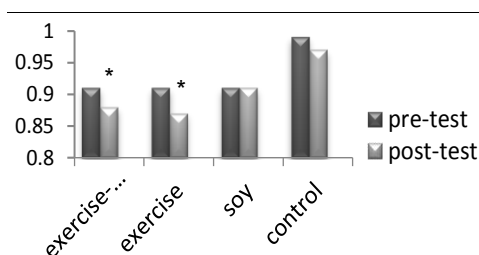
results of variance analysis showed that the effect of exercise ($p = 0/012$) and the interaction of exercise - soybean ($p = 0/024$) is significant on the distribution of the mean difference of weight. It seems that a significant change of these variables has been under the influence of exercise and synergistic effect of exercise plus Soya (Figure 1: c). LSD post hoc tests showed that there is significant difference in mean difference of the distribution between Control and exercise groups ($p = 0/05$). The maximum degree of reduction of this index was related to exercise group.

Fat percent

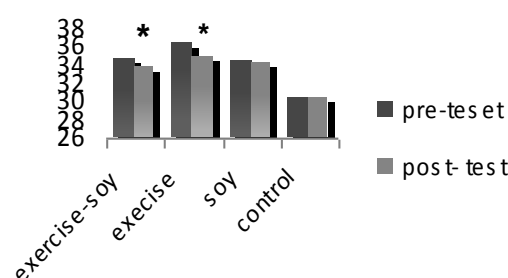
results of variance analysis showed that the effect of Soya and exercise and effect of exercises-soy on the distribution of the mean difference was not significant ($P > 0/05$) (Figure 1: d).

17 β -estradiol

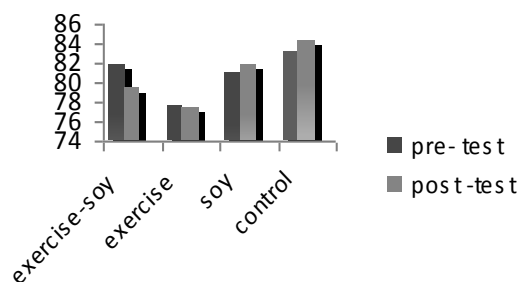
Results of variance analysis showed that the effect of exercise ($p = 0/04$) and the interaction of exercise - soybean is significant ($p = 0/03$) on the distribution of the mean difference. It seems that a significant change of this variable has been under the influence of exercise and synergistic effect of exercise plus Soya (Figure 1: e). LSD post hoc tests showed that there is significant difference in mean difference of the distribution between control groups and exercise - Soy, Control and exercise groups ($p = 0/05$). The maximum degree of reduction of this index was related to exercise - Soy group.



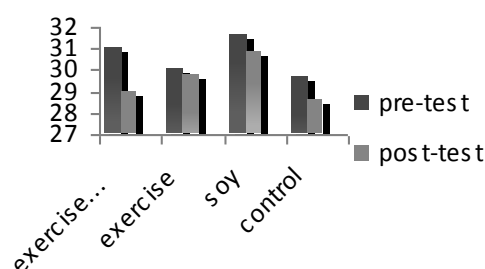
(a): Waist to hip ratio measured at baseline and following 10 weeks of soy intake and aerobic exercise* Significance of the pretest values in both groups ($p < 0.05$)



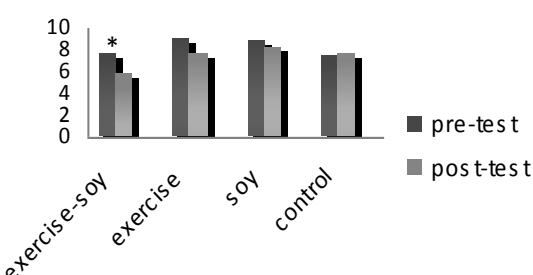
(b): BMI (kg/m²), measured at baseline and following 10 weeks of soy intake and aerobic exercise. * Significance of the pretest values in both groups ($p < 0.05$).



(c): Weight (kg) measured at baseline and following 10 weeks of soy intake and aerobic exercise. At week 10, groups analysis shows no significant Decrease in weight ($p > 0.05$).



(d): Fat percent measured at baseline and following 10 weeks of soy intake and aerobic exercise. At week 10, groups analysis shows no significant Decrease in body fat percent ($p > 0.05$).



(e): 17β-estradiol (pg/ml), measured at baseline and following 10 weeks of soy intake and aerobic exercise. * Significance of the pretest values in both groups ($p < 0.05$).

Fig. 1. (a): Waist to hip ratio, (b): BMI (kg / m²), (c): Weight (kg), (d): Fat percent, (e): 17β-estradiol (pg/ml) measured at baseline and following 10 weeks of soy intake and aerobic exercise. At week 10, exercise-soy group analysis shows a significant Decrease in Waist to hip ratio ($.91 \pm .06$ to $.88 \pm .08$), BMI (34.56 ± 7.04 to 33.61 ± 6.1 kg / m²), and 17β-estradiol (7.62 ± 2.12 to 5.84 ± 3.76 pg/ml) ($p < 0.05$). exercise group analysis shows a significant Decrease in Waist to hip ratio ($.91 \pm .09$ to $.87 \pm .05$) & BMI (36.21 ± 2.54 to 34.93 ± 6.87 kg / m²) ($p < 0.05$).

* significance of the pretest values in both groups ($p < 0.05$).

Discussion

High levels of serum estradiol in postmenopausal women are associated with increasing of breast cancer risk (Anne *et al.*, 2007; Timothy, 2003). Several studies have been shown the reduce of

estradiol and obesity by physical activity (Verkasalo, 2001; Tiernan *et al.*, 2004; Napieralski, 1999). On the other hand, soy consumption also is effective in reducing serum estradiol and risk of breast cancer (Marianne *et al.*, 2008; Christine *et al.*, 2007; Maesta *et al.*, 2007). In the present study which also the effect of soy consumption combined with aerobic activity were examined, decreasing of serum estradiol concentrations after 10 weeks of aerobic exercise at moderate intensity in "exercise-Soy" and "exercise" groups represents effective role of training program in reducing serum estradiol. Anne MC & *et al* and Tiernan & *et al* and Julie A Napieralski Studies have shown the effect of moderate intensity of exercise program in reducing women serum estradiol (Tiernan *et al.*, 2004; Napieralski, 1999; Anne, 2006). Also in the present study, Incremental effect of intervention in both "exercise & soy" on estradiol compared with exercise group (Figure 1) could indicate the role of soy in the increase effect of the training program in reducing serum estradiol. The role of soy in reducing serum estradiol, Lee Jane W showed that women who consumed soymilk for one month had a 20% reduction in serum 17β -estradiol concentration (Lee - jane *et al.*, 1996). Reviewing of several studies also showed the decreasing of serum estradiol with Soya daily consumption in women (32 to 200 mg Isoflavones) (Persky *et al.*, 2002). Soy is well known for its estrogenic effects, which may occur through the hypothalamic-pituitary-gonadal axis. Isoflavones inhibit key steroidogenic linked enzymes including aromatase enzyme, 17β -hydroxysteroid oxido reductase and cytochrome p-450 with the latter responsible for estrogen hydroxylation (Kalman *et al.*, 2007). These postulated mechanisms provide a probable rationale for the decline in serum estradiol across all soy groups within the current study (Figure 1). However, there are studies in which Soya consumption alone is not effective in reducing serum estradiol. In the present study, serum estradiol in the Soya group did not change significantly after 10 weeks of soy consumption that these findings were in line with results of Yuan J M,

Wang QS, Nailza Maesta Kok L, Williams AE, Maskarinec G studies. Perhaps one of the mechanisms that present aerobic exercise program lead to a decrease in serum estradiol was decrease of the obesity in postmenopausal obese women (Napieralski, 1999) that in the present study, BMI in the "exercise - Soya" and "exercise" group was significantly decreased. It seems that significant changes of these variables have been under the influence of exercise and the synergistic effect of exercise - soy. In examining the relationship between body mass index and sex hormones in postmenopausal women, study of Anne MC& *et al* and Tiernan & *et al*, showed that obese women (BMI > 30 kg/m²), had more serum concentration of 17β -estradiol (130%) than lean women (BMI < 22) (Anne *et al.*, 2003). This study found no significant decrease in fat, but waist to hip ratio was significantly decreased in the "exercise-soy" group and body weight in the "exercise - soy" and "exercise" group. These results shows the indirect effect of exercise program in reducing obesity and serum estradiol. However, there are studies that despite a significant losing in weight, serum estradiol concentrations have not decreased significantly that this relates to factors other than physical activity in losing body weight. For example in Nancy Williams's studies which the effect of 8-week exercise program and reducing of energy consumption in non-menopausal women were reviewed, despite a significant losing in weight and fat subjects, serum estradiol levels were non-significantly lower and part of weight loss, was because of energy intake reduction (Maesta *et al.*, 2007). Nevertheless, what in present study and previous studies (Anne, 2004 and 2006; Napieralski, 1999; Maesta *et al.*, 2007) in this area is evident, was losing weight, body mass index and waist to hip ratio associated with significant reduction in serum estradiol. Moderate intensity physical activity (60 to 70 percent of maximum heart rate reserve) through mechanisms such as changes in fat distribution in fat tissue, Estrogen-induced reduction of adipose tissue, activation of enzymes that convert estradiol to estrone (E1) and

changing of estrogen metabolism, body weight and body fat percentage loss plays a significant role in reducing risk of breast cancer in the body (Napieralski,1999). These mechanisms reflect the independent and indirect role of physical activity in decreasing serum estradiol. Although in the present study, Soya alone had no role in reducing obesity and serum estradiol but cannot be ignored the synergistic effect of Soya + exercise in reducing body mass index and waist to hip ratio and serum estradiol concentration. Soybeans due to having fiber and satiety and metabolism increase of fat, is considered a good source of dietary fat in the treatment of obesity and reduction of high blood lipids in obese (Liao *et al.*, 2007; Benoit *et al.*, 2009). In 2003 Goodman Gruen and Kritz-Silverstein studied body fat percentage of 208 women, 45-74 years old, observing a decrease in total body fat with soy consumption, they concluded that soy plays a role in reducing obesity (Eliana *et al.*, 2006). The results of two studies that were studied effect of isoflavones consumption in postmenopausal women, showed that women who used more isoflavones compared with low consumers of isoflavones, had favorable waist to hip ratio (Teresa *et al.*, 2004). Soy capacity is in weight regulation and lipid metabolism of the amino acid building and other components. Recent studies have shown that soy protein decreased expression of sterol regulatory element binding protein-1 and prevents the expression of lipogeny genes and fat accumulation and lead to decreasing body fat (Liao *et al.*, 2007). Therefore, in explaining more effective role of aerobic training of present study with soy consumption in reducing serum estradiol, we can say that moderate intensity physical activity with soy intake through mechanisms such as losing obesity; can play a significant role in reducing the risk of breast cancer.

Declaration of interest

Authors declare no conflict of interest.

Conclusion

Overall, this study showed short-term moderate intensity aerobic exercise along with taking Soybean can reduce risk of breast cancer with reduction of 17 β -estradiol, body mass index and waist to hip ratio in postmenopausal women. So in order to increases the effect of exercise and soy intake on decrease of body fat percent recommended in extensive study of large and available samples of premenstrual women, with non-limits in intensity and duration of exercise training.

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