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The Relationship between Estrogen and Lipid Profile in Follicular Phase of Active Women

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Abstract

Introduction: Estrogen is the basis of pregnancy and is involved in many physiological activities. Regarding the effects of exercise on lipid profile and estrogen, the aim of this study was to investigate the relationship between estrogen and lipid levels in active women.

Methods: From among female students of Islamic Azad University of Masjed-Soleiman, after examining the conditions of inclusion and signing consent form, 38 inactive women (age: 26.1 ± 6.27 y; BMI: 24.2 ± 2.4 $kg.m^{-2}$) and 31 active women (at least 150 min activity per week; age: 27.68 ± 5.72y, BMI: 22.3 ± 65.64 $kg.m^{-2}$) participated in study. In the late folicular phase, 3-cc blood was taken from the subjects in the fasting state. HDL, LDL, TG, cholesterol and estrogen (17 Beta-estradiol) were measured during four months. Pearson correlation and sample t-test for statistical analysis was used. The significance level was $p < 0.05$.

Results: The results showed in active women there was a significant inverse relationship between estrogen and cholesterol (P = 0.01) and TG (P = 0.02). Comparing the groups, the levels of cholesterol (P = 0.0001), LDL (P = 0.0001) and TG (P = 0.01) in active woman were significantly lower than inactive women.

Conclusion: The results of our study showed that measurement of estrogen and blood lipids in different times of menstrual cycle was different in active and inactive women. Therefore, regarding the enormous effects of endogenous estrogen on health, it is recommended that women maintain a good level of activity per week in order to benefit from its health benefits.

Keywords: Menstrual Cycle, Estrogen, Lipid Profile

Introduction

Nowadays, exercise as a remedial tool in the field of medical science has a special position in the treatment of physical and mental disorders. Millions of people worldwide are presently suffering from chronic illnesses that can be improved by physical activities (1). Low activity is a major contributor to cardiovascular diseases (2). Zachariah and Alex (2017) concluded that physical activity not only sport-related activities but also lifestyle-common activities significant reductions in cardiovascular-related mortality. They recommended 30 min of moderate intensity exercise on most days of the week (equivalent to 4.2 MJ/week or 1,000 kcal/week) (3). Women experience increased cardiovascular problems when they lose estrogen levels. Research has shown that performing sports activities that are high intense and short-term will compensate for estrogen reductions. Significantly change estrogen metabolism with exercise decreases blood pressure and improves the cardiovascular system (4). Research has shown that inactive lifestyle along with a high-fat and high-calorie diet may trigger and exacerbate cardiovascular disease by altering metabolism status and lipid profile, especially peripheral blood lipoproteins (5). In addition, studies have shown that 1% (1 mg/dl) reduction of cholesterol in low density lipoprotein (LDL-C) plasma levels decreases about 2% mortality rate from atherosclerotic cardiovascular disease (5). Some researchers have studied estrogen changes and lipid profile

in relation to menstruation in women. So far, little research has been carried out on the above-mentioned subject and research has often focused on estrogen levels and their relationship with health factors in postmenopausal women. Mumford *et al*. (2010) showed that cholesterol and triglyceride have a negative correlation with estrogen and have a significant positive correlation with HDL (6). El Khoudary *et al*. (2014) found that estradiol positively correlated with HDL size and had negative correlation with medium-small LDL particle (7). As noted, some researchers believe that changes in lipid profile in women are related to changes in estrogen in the menstrual cycle. Also, studies on the effect of physical activity on cardiovascular risk factors show that physical activity improves lipid profiles and estrogen metabolism (4, 8- 10). Now, there is a question about how estrogen interacts with lipid profiles change in menstrual cycles in active women. The study conducted by Lamon-Fava *et al*. (1989) on runner women without amenorrhea indicated that the estrogen levels were similar to the control group and had a positive association with Apolipoprotein A-I (11). While the relationship between estrogen and lipid profile in active women in the menstrual cycle has been studied in little research, the purpose of this study was to investigate the relationship between estrogen and lipid profile in follicular phase of active women.

Methods

From among female students of Islamic Azad University of Masjed-Soleiman, after examining the conditions of inclusion and signing consent form, 38 inactive women and 31 active women participated in this study. Active subjects were referred to individuals who had regular sports activities at least in the last year, and at least did 150 minutes a week exercise with moderate to high intensity (12). On the other hand, inactive subjects were referred to individuals who did not have any regular sports activities during the last year. Inclusion criteria included: The age range is 18-40 years, not having menstrual disorders, not pregnancy, no smoking or drinking alcohol; do not use any medication or supplement, having any medical precautions to participate in the research, any physical or mental disorder. Exclusion criteria included: cancellation of participation in the research, failure to recognize ovulation time, consume any medication or supplement to your doctor's diagnosis, incidence of the disease, pregnancy. After the sample declared preparation, each subject was given ovulation timing form and special ovulation kits. Each subject was asked to record the number of days of her periodic cycle and the approximate time of ovulation in the first month, considering her ovulation symptoms such as pain in the oocyte, changes in vaginal secretions and temperature changes. In the second month, with an approximate estimate of the time of ovulation and the approximate time of its diagnosis through existing brochures, after the end of the monthly bleeding period, the time for late follicular phase was determined using the special kits for ovulation. After the two test lines were painted, the subjects in the fasting state referred to Pars Masjed-Soleiman lab in the next morning, and 5 cc of blood was taken from the left hand of each subject. Blood samples were centrifuged to measure the lipid profile (LDL, HDL, TG and cholesterol) and estrogen and were maintained at -20 ° C until the completion of experiments. Measurement of lipid profile was performed with enzyme method using commercial kits of Pars Azmoon (manufactured in Iran); and to measure the concentration of beta estradiol, Monobind Company kit (manufactured in America, Product Code: 4925-300) with a sensitivity of 6.5pg/ml was used in accordance with the catalog kit. Data were developed using descriptive statistics. The normal distribution of data was done by Kolmogorov-Smirnov test. To investigate the relationship between the variables of the research, Pearson

correlation was used and to conduct comparison of the two groups, independent sample t-test was run, using SPSS software version 19. The significance level was considered as $p < 0.05$.

Results

In the active group, the mean and standard deviation of age 27.7±5.7 years, height: 164.8 ± 4.9cm, weight: 61.4±9.1 kg and body mass index: 22.7±3.6 kg/m^2 was. In the inactive group, the mean and standard deviation of the age 26.1±6.3 years, height: 161.3 ± 6.3cm, weight: 62.5 ± 7.7 kg, and body mass index: 24 ± 2.4 kg/m^2 was. The mean ± standard deviation of lipid profile and estrogen of the two groups can be seen in Table 1. The analysis of the relationship between estrogen and each lipid profile is shown in Table 2. The results of the comparison of lipid profile in the two groups showed that there was a significant difference between levels of cholesterol (P = 0.0001), LDL (P = 0.0001) and triglycerides (P = 0.01), so that the cholesterol, LDL and TG levels were lower in the active group compared to the inactive group. On the other hand, HDL (P = 0.18) did not show a significant difference between active and inactive groups (Fig. 1). Figure 2 also shows that there is no significant difference between estrogen levels (P = 0.19) in the two groups.

Table 1. *Levels of blood biochemical factors in the subjects of two groups*

Variable	Active group	Inactive group
Cholesterol (mg/dL)	144.24±69.64	194.31±00.29
Triglyceride (mg/dL)	74.14±02.90	109.58±69.31
HDL (mg/dL)	46.8±96.96	50.12±94.86
LDL (mg/dL)	83.23±38.97	110.27±20.23
Estrogen (Pg/mL)	173.50±06.67	152.68±79.98

Table 2. Correlation matrix and Pearson coefficient of estrogen level with blood lipids in both groups

Variable		The statistics	Cholesterol	Triglyceride	HDL	LDL
Estrogen	Active	Correlation Coefficient	-0.48	-0.46	-0.36	-0.02
		Sig.	0.01	0.02	0.07	0.94
	Inactive	Correlation Coefficient	0.17	0.3	-0.1	-0.01
		Sig.	0.33	0.08	0.56	0.95

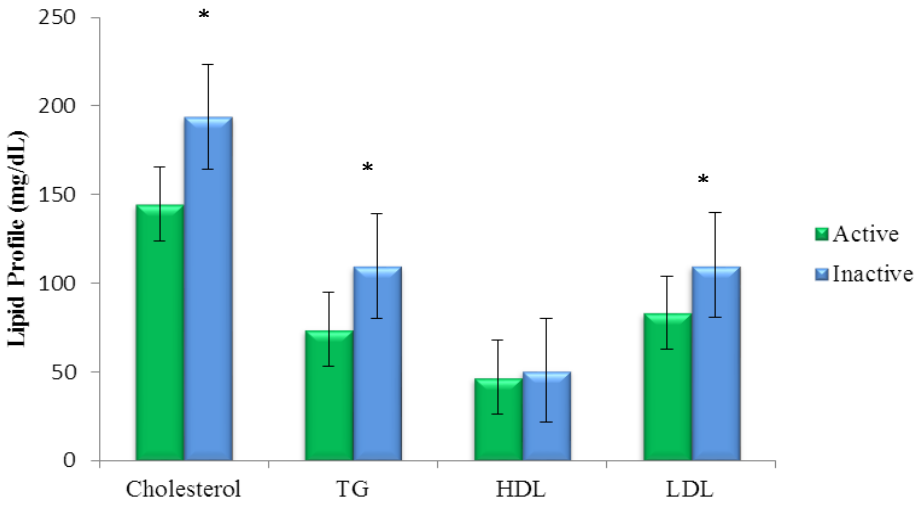

Figure 1. Comparison of blood lipids profile in active and inactive groups
*significant difference between active and inactive groups (P < 0.09)

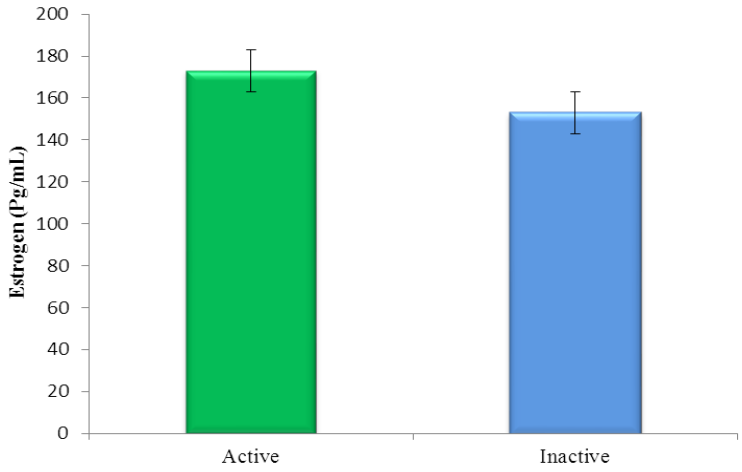

Figure 2. Comparison of estrogen levels in active and inactive groups

Discussion

The purpose of this study was to determine the relationship between estrogen and serum cholesterol, triglyceride, HDL and LDL levels in active and inactive individuals in the late follicular phase. The above levels, which are included in risk factors of cardiovascular disease, were shown to have statistically significant relationship with estrogen in the active group (significant relationship between estrogen and triglyceride and cholesterol), while this connection was not significant in the inactive group. Also, the rate of lipid profile in the active group was lower than the inactive group, but there was no difference in the levels of estrogen and HDL between the two groups. In agreement with the results of this study, Mumford *et al*. (2010) in 12 women aged 19 to 37 years showed that cholesterol and triglyceride had a significant negative correlation with estrogen (6). El Khoudary *et al*. (2014) in one hundred and twenty women (57.5% white and 42.5% black) who were 50.4 ± 1.9 years old after adjusting for age, race, cycle day of blood draw, BMI, physical activity, and alcohol consumption found negative correlation between Estradiol with medium-small LDL particle (7). In contrast to the results of this study, El Khoudary *et al*. (2014) found estradiol positively correlated with HDL size (7). Wall *et al*. (1994) showed that HDL has a significant positive correlation with estrogen after eliminating the effect of age, BMI, waist to hip ratio and race (13). Also, they showed a positive and significant relationship between HDL and estrogen in the ovulation phase. Lamon-Fava *et al*. (2005) evaluated the relationship between HDL and estrogen positively and significantly after eliminating the effect of age, BMI, and waist to hip ratio in two African-American and Caucasian races (14). Also, Mumford *et al*. (2010) showed positive relationship between HDL and estrogen (6). The research conducted on healthy women before menopause showed a positive relationship between estrogen and HDL, while in the present study a significant relationship between estrogen and HDL was not observed in active and inactive women, in separate or totally. It seems that base of some research the highest peak in HDL is in and luteal phases (15), thus the lack of significance may be partly due to HDL measurement in the follicular phase. It also seems that change in HDL levels due to activity requires a prolonged time, the amount, type, and certain severity of the activity (9, 16). In the present study, active women were selected from among women who were engaged in activities such as gymnastics, taekwondo, karate, badminton and basketball, which due to their low-aerobic nature, their effects on HDL may

have not been very noticeable; consequently, the results showed that in the active group the levels of HDL only in 19% of the subjects were favorable, and in 69% of the subjects low levels of HDL were shown. Other reasons for not observing the relationship may also be attributed to the not-so-increased estrogen levels, because there was no significant difference between estrogen levels in the active and inactive groups. Investigating the relationship between estrogen levels and lipid profile in healthy women has shown that cholesterol and LDL levels in the follicular phase are higher and decrease during luteal phase (6), while HDL values in the ovulation phase increased when progesterone levels were low (6, 17). Although studies have shown that HDL and triglyceride levels are higher in luteal phase and ovulation than follicular phase. Also, LDL and cholesterol levels were higher in the luteal phase than follicular. The results of this study are related to increased levels of estrogen in the luteal phase (18). In fact, most women seem to have shown the desired levels of cholesterol and LDL in the ovulation phase. Estrogen also has an acute, rapid increase in HDL, but this acute effect is not known about LDL and cholesterol (6). In the studies conducted in the middle follicular phase, there was a positive correlation between estrogen and HDL, while no relationship was found with cholesterol and LDL, and cholesterol and LDL levels were lower in the luteal phase (6). Factors such as level of activity, type of nutrition, age, weight, percentage of fat and race may cause significant differences in the results of the research. Estrogen secreted from the ovaries is responsible for the characterization of secondary sexual characteristics in women. 17 Beta-estradiol is the greatest and the most important type of estrogen; its amount changes during the menstrual cycle, and its highest value is before ovulation prior to the late follicular phase. Estrogen is the basis of pregnancy and participates in many physiological activities such as cardiovascular function, respiratory function, substrate metabolism and energy sources, body composition, weight control, mineral density, body temperature regulation, and psychological factors (19). Estrogen also affects skeletal-bone tissue injuries, power and strength, aerobic and anaerobic capacity, and psychomotor factors (19). The effects of this hormone is important for examining menstrual disorders, delayed puberty, primary and secondary amenorrhea, and menopause. Lack of long-term estrogen reduces the concentration of minerals causing osteoporosis in menopause. Also, as mentioned earlier, estrogen effects on cardiovascular disease and lipid profile have been proven (20). Researchers have found that estrogen upregulates mRNA expression of SR-BI, the HDL receptor, and promotes HDL cholesterol uptake in peripheral tissues (21, 22). Therefore, estrogen regulation of HDL uptake by the liver may contribute to the sex difference in cardiovascular risk (23). Estrogen also increases the VLDL liver subset that lacks vascular adhesion and generally has beneficial effects on health (24). While the use of contraceptive pills that contain some kind of exogenous estrogen leads to an increase in triglycerides and lipoprotein composition, and inflammatory and hemostatic markers (25, 26). Physical activity seems to have beneficial effects on health through increased estrogen levels in active and athletic individuals. As the results of the present study showed active women had lower risk factors for cardiovascular disease than inactive people, yet the affecting mechanisms of exercise on lipid profile have not been known. Physical activity seems to increase the ability of the musculoskeletal system to use lipids instead of glycogen, thus reducing plasma lipid levels (27). This mechanism may include an increase in lecithin–cholesterol acyltransferase **(**LCAT)**,** the enzyme responsible for transmitting esters to HDL cholesterol (28), which has been shown to increase after exercise (29), and it also increases lipoprotein

lipase activity (30) and may be related to energy consumption during activity.

Conclusion

The results of the present study showed active women had lower risk factors for cardiovascular disease than inactive people. The increased levels of estrogen in active women were not significant compared to inactive women; the same insignificant increased levels were associated with a decrease in cholesterol and triglyceride levels, indicating the benefits of physical activity in women.

Ethical issues

Not applicable.

Authors' contributions

All authors equally contributed to the writing and revision of this paper.

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