Original Article

Effect of exercise on sex-hormone in rats with polycystic ovary syndrome

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Abstract

Introduction:
Weight gain and fat accumulation are the risk factors which lead to polycystic ovary syndrome. The aim of this study was to examine the effect of exercise intensity on sexual hormone changes in rats with polycystic ovary syndrome.

Materials and Methods:
40 female Wistar rats (180±20mg) with 2 to 3 consecutive estrous cycles during12 to 14 days were selected. The first two groups were divided into control (n=30) and polycystic (n=30) that got sick by estradiol valerate injection after 60 days. The polycystic groups were divided into three groups of observer (n=30), experiment group1 (low-intensity exercise (n=30)) and experiment group 2 (moderate intensity exercise (n=30)). Exercises were performed in 6 sessions of 60 minutes per week for 8 weeks. The mice were anesthetized by injection of 5 ml of blood directly from the heart and the blood factors were measured through Elisa; ANOVA and LSD samples were used for normal distributions and Kruskal-Wallis test for analysis of data that were not normally distributed.

Results:
Concentrations of FSH in experiment group1increased significantly compared to the control and observer groups. Also, free testosterone was significantly higher as compared to the observer group. FSH concentration in group 2 was higher as compared to the control and observer groups, and changes to LH, estrogen and androstenedion were not significant compared to the control group despite their increase.

Conclusion:
According to weight changes and sexual hormones (FSH and Androstenedion) exercise, especially with low intensity, may improve the symptoms of polycystic ovary syndrome.

Keywords: Exercise, Polycystic Ovarian Syndrome, Sex Hormone, Rats

Introduction

The importance of exercising for physical and psychological health of members of the society is completely evident and is known as an inseparable part of the physical and psychological health. It is vital to pay attention to women's exercise as a major part of the society considering their physiological needs and conditions (1). Physical activity and exercise increase or decrease some hormone levels compared to resting time. Although the physiological importance of many of these changes is currently unknown, the fact that

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hormone levels react to exercising is utterly important (2).

Infertility is definitely one of the major problems in medicine, such that its prevalence has increased since 1955 in the world and currently 10-15% of couples suffer from it (3). One of the most common causes of infertility is polycystic ovary syndrome (PCOS), accounting for the 20% of couples' infertility causes, and 6-8% of women in reproductive age suffer from endocrine disorders (4-5). PCOS is a heterogeneous set of signs and symptoms which range from mild to severe reproductive, endocrine and metabolic function disorders. This syndrome is a multifactorial disorder which is thought to have genetic etiology, but its intensity and duration are determined by a change in the lifestyle, particularly, the body mass index. Most women (80-90%) who do not ovulate suffer from ovarian hyperstimulation syndrome (6). The important symptoms of this syndrome include irregular menstrual cycles, abnormal growth of facial hair, infertility, weight gain, polycystic ovaries, increased androgen (clinical or biochemical), anovulation or oligovulation, hypothalamus dysfunction, pituitary dysfunction, and ovarian dysfunction (increased LH and decreased FSH), decreased estrogen and increased testosterone levels and other identifying factors (6-7). Medication is often recommended for treating this sickness, and non-medical therapies include dietary limits and physical activity (8-9).

Exercise and physical activity reduce the body fat where estrogen is stored and steroid hormones are produced (10). Researchers believe that regular and medium intenstiy exercise is a healthy and natural treatment for this group, apart from clinical treatments (11). In a study about the effect of physical exercise on the hyperandrogenism, oligo/amenorrhea and amenorrhea in 84 randomly selected women with PCOS showed that the androgen and other estrogenic hormone levels and also 17-beta estradiol reduced and menstrual frequency improved as a result of exercising. The intensity of exercises was not specified in this research, though (12). Also, examining the effects of aerobics on PCOS showed that it changed sex hormones in addition to body fats (13). Previous studies about regular exercise with high-intensity (80-85% maximum consumed oxygen), moderate-intensity (70-75% maximum consumed oxygen) and low-intensity (50-55% maximum consumed oxygen) showed that the testosterone concentration is lower in the high-intensity group than in the control sedentary group (14). It was also stated in 2011 that exercise can increase ovarian hormones, indicating that the mechanisms related to ovarian disorder can improve with exercise (15).

Due to the importance of exercise for the treatment of many diseases, including female hormonal diseases and as there are no studies about the effect of the intensity of exercise on the treatment of PCOS, the present study was conducted on the effect of endurance exercises with low- and moderate- intensity on the treatment of PCOS induced in adult female rats.

Materials and Methods

This experimental research was conducted in a laboratory environment, and all ethical principles about working with laboratory animals were observed. Forty female Wistar rats weighing 180±20 g, aged 80-90 days were acquired from the Research Center of Shiraz University of Medical Sciences. The rats were kept in the animal house of Jahrom Islamic Azad University for two weeks in the standard laboratory conditions (23± 2° C temperature and 12-hour light/dark cycles). The rats were kept in plexiglass cages with grid doors and they were fed rat feed (obtained from Shiraz Livestock and Poultry Company). The rats were given water through particular glass bottles. Their cages were disinfected 3 times a week with alcohol 70%.

Method for PCOS Induction

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There are various hormonal and non-hormonal methods for induction of PCOS phenotype, such as the testosterone hormone, estradiol valerate, dehydroepiandrosterone, adrenocorticotropin and using long-term light (16-19). A hormonal induction method with estradiol valerate was used in this research. The rats that had 2-3 regular estrous cycles during a period of 12-14 days were selected for this study after daily vaginal smear test. From the 40 rats with regular estrous cycles, 30 rats were randomly selected and all except the normal control group were injected with 4 mg/kg body weight which was dissolved in sesame 0.2mg of oil as solvent (17,20). For verifying the induction of PCOS in the experimental groups and reaching a persistent vaginal cornification, daily vaginal smear was taken for 60 days (16-17).

Measuring Physical Activity and Setting the Treadmill

Using Sheperdogolnic's study (1976) about rodents, the time that each rat needed for running on the treadmill was measured with 65-70% maximum consumed oxygen intensity (28 meters per minute). To adjust the likely changes of the treadmill speed due to transferring the rodents' treadmill to the laboratory environment, initially its belt was measured with a tape measure and then a point was marked on it as the criterion. Then, the time spent for a complete rotation of the belt was measured and entered into the speed formula and the result was compared to the machine's electric monitor

The study variables include independent and dependent variables as follows:

The independent variables consist of physical activity with low-intensity (20 meters per minute) and with moderate-intensity (27 meters per minute) (35). The dependent variables include the levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), free testosterone and estrogen hormones whose changes will be assessed at the end of the test.

After verifying the induction of PCOS, the animals were randomly divided to three groups of 1-The normal control group (10 adult female rats without receiving any substance or taking any exercise), 2- the sick control group (10 adult female rats with PCOS without taking any exercise), 3- the low-intensity exercise experimental group (10 adult female rats with PCOS) and 4- the moderate-intensity exercise experimental group (10 adult female rats with PCOS).

In the first week, the low- and moderate-intensity exercise groups walked on the treadmill. The speed's changes and the different stages of the rats' acquaintance with the treadmill are presented in table 1.

Table 1: The different stages of the rats' acquaintance with the treadmill machine

week	Time (minute)	Slope%	Speed (meter per minute)	
			Group 1	Group 2
1	30	0	20	20
2	40	0	20	27
3	50	8	20	27
4	50	8	20	27
5	60	8	20	27
6	60	8	20	27
7	60	8	20	27
8	60	8	20	27

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The exercise practices continued for 8 weeks. After 32 hours from the last exercise session and 12 hours of fasting by the rats, all groups of the rats were dissected and 5 CC blood was collected from their hearts with syringes. After separating blood serum, the concentrations of luteinizing hormone stimulus (LH), follicle-stimulating hormone (FSH), free testosterone and estrogen were measured by Elisa method in the laboratory of Jahrom University of Medical Sciences. On-way variance analysis was used to compare the mean and the standard deviation of hormones in studied groups; then the Tukey test was used for the multiple comparison of different groups. $P<0.05$ was considered as the statistically significant level. In the present research, all data show a normal distribution according to the Kolmogorov–Smirnov test ($P>0.05$). The Kruskal-Wallis test was employed for the multiple comparison of the LH hormone data ($P<0.05$). The SPSS-18 software was used for testing the hypotheses and analyzing the data and the Excel program was used for drawing the charts and figures and for describing the data.

Results

The result of research showed FSH level in the low-intensity exercise experimental group as figure 1 illustrates, is significantly higher than in the healthy and sick control groups ($P<0.05$). But according to figure 2, LH level is not significantly higher in the low- and moderate-intensity exercise experimental groups than in the healthy control group. The free testosterone level, as figure 3 shows, is significantly higher in the moderate-intensity exercise experimental group than in the sick control group and also the low-intensity exercise experimental group shows a decrease that is not significant ($P<0.05$). The estrogen level, as figure 4 illustrates, shows an insignificant increase compared to the healthy control group ($P<0.05$).

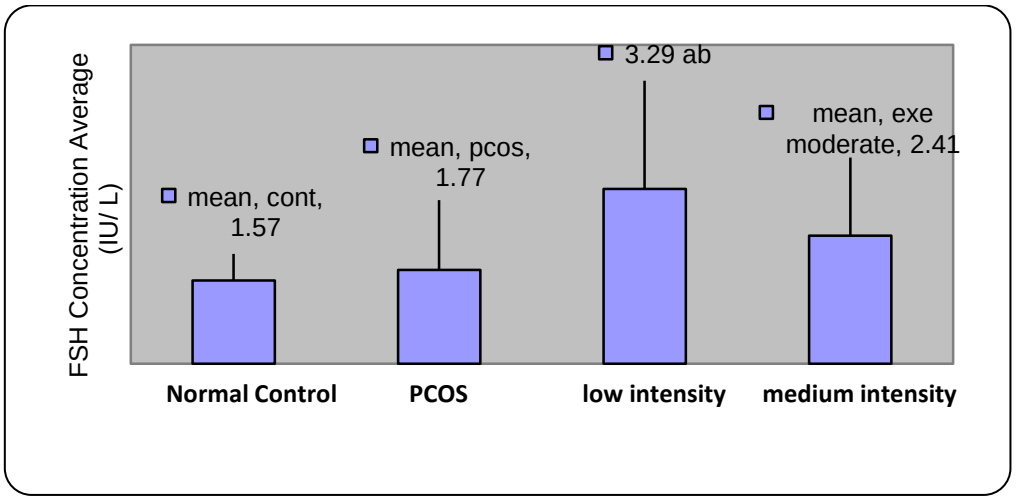

Figure 1: The comparison of the mean of the FSH levels in the control and experimental groups (IU/L)

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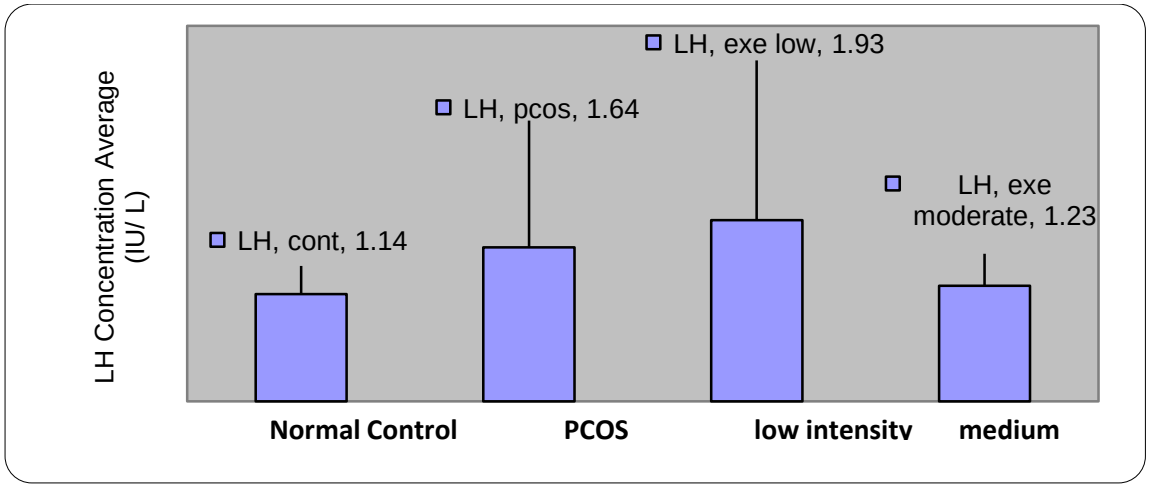

Figure 2: The comparison of the mean of the LH levels in the control and experimental groups (IU/L)

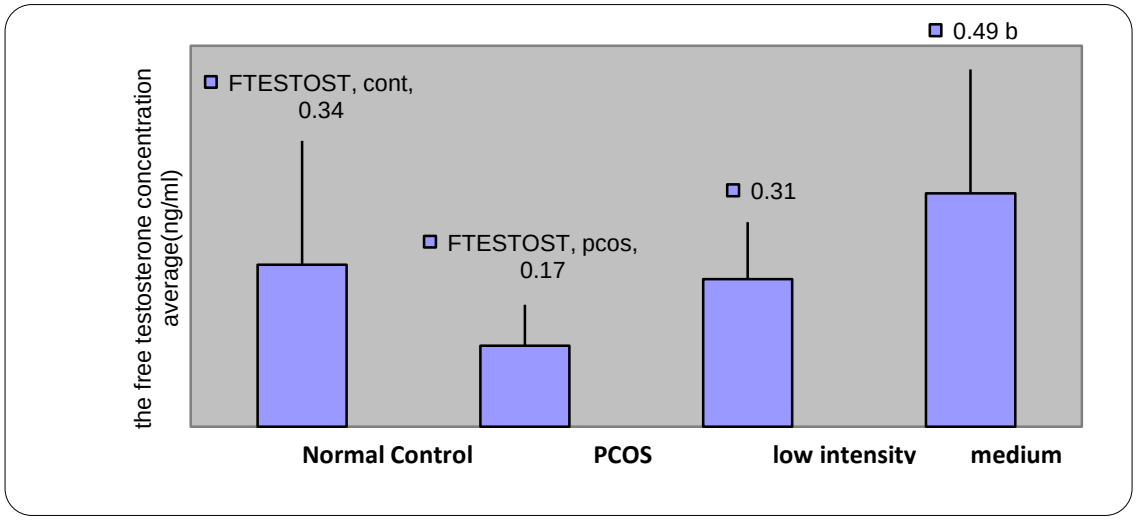

Figure 3: The comparison of the mean of the free testosterone levels in the control and experimental groups (ng/ml)

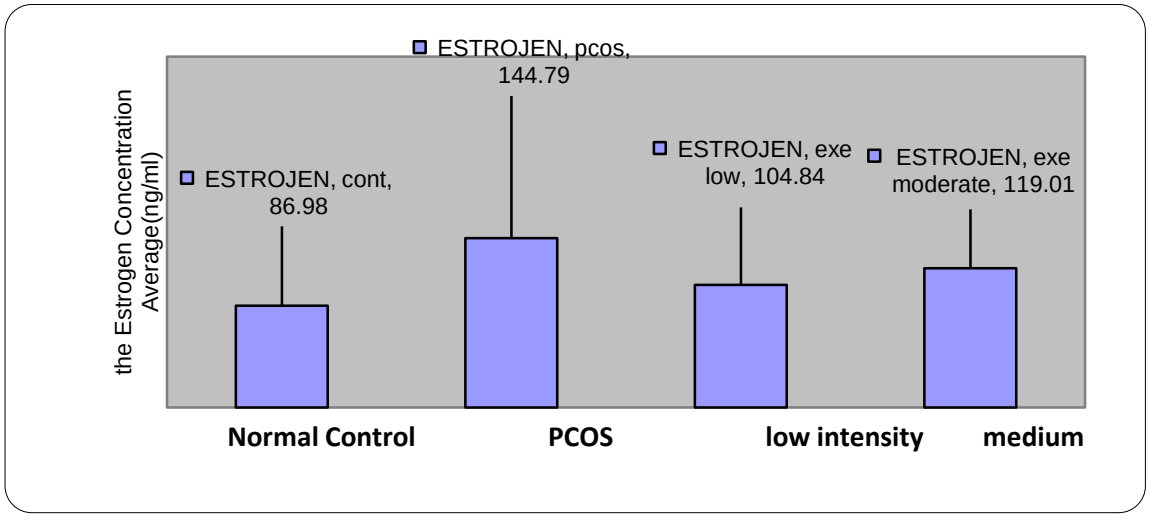

Figure 4: The comparison of the mean of the testosterone levels in the control and experimental groups (ng/ml)

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Table 2: The comparison of the mean of LH and FSH, free testosterone and estrogen levels in the control and experimental groups of the rats

	Control	PCOS	Low intensity	Moderate intensity	Fisher Value	Significance Level
FSH(IU/L)	1.5730±0.5	1.77±1.3	2.416±2.04ab	3.29±+1.47	2.785	0.056
LH (IU/L)	1.142±0.3	1.648±1.35	1.933±1.7	1.237±0.34	1.036	0.389
(ng/ml)Free testosterone	0.343±0.26	0.178±0.08	0.319±0.12	0.494±0.26b	0.015	0.015
Estrogen (ng/ml)	86.98±67.99	144.79±121.53	104.844±66.22	119.01±50.56	0.875	0.464

a: a significant difference compared to the control group (P<0.05)
b: a significant difference compared to the PCOS group (P<0.05)

Discussion

The definitive results of exercise intervention for the treatment of PCOS symptoms are still unknown. An experimental study showed that in overweight women with PCOS and ovarian disorder, exercise could regulate their ovarian hormones balance. This indicates that the mechanisms related to ovarian disorders could improve with exercise (15).

Studies show that hyperandrogenism and the increased serum levels of LH and testosterone are common in this disease (21-22). Other studies in the field show that endurance exercise with different intensity levels can increase and balance the FSH level, though these changes have not been significant (23-25). In the present research, as figure 1 illustrates, the FSH level is significantly higher in the low-intensity exercise group than in the control and PCOS groups, showing the positive impact of low-intensity exercise on the changes of the FSH in the PCOS group.

According to previous studies, exercising with a fixed intensity decreases the FSH level slightly, which is incompatible with the current research's results. The reason for this phenomenon might be the length of the treatment period, the exercise intensity used in this research, the use of animal samples, different ways of exercising, and the length of exercising time (30). As figure 2 depicts, the LH level has insignificantly increased in the low-intensity experimental groups, while decreasing insignificantly in the moderate-intensity exercise group, showing the positive effects of moderate-intensity exercise on the LH level. Another study on the effects of exercise on women with PCOS points to the decreased level of LH, which is inconsistent with the present study results. However, LH changes in the present research have not proved significant (26).

Generally, gonadotropins are glycoproteins that release from hypophysis in response to gonadotropin-releasing hormones (GnRH). The pulsatile release of GnRH causes the pulsatile production of LH and FSH concentrations (27). Studies show that exercise increases individuals' beta-endorphin level, which in turn, decreases GnRH followed by a decrease in LH level (27). The decrease in LH level in the moderate-intensity exercise experimental group compared to the PCOS group was not significant in this research, but it shows the positive impacts of moderate-intensity exercise on the hormonal changes in the PCOS group. Estrogen and LH levels did not significantly change in this research, though. It is also stated that high-intensity exercising in untrained people would remarkably increase their sex hormone levels (30).

It seems that exercise with low-intensity and longer time is more effective on hormonal changes. The increased free testosterone level can be due to a decrease in the amount of sex hormone-binding globulin (21-22). On the other hand, increased free testosterone level in the 60 minutes daily moderate-intensity exercise experimental group can be attributed to the fact that this hormone is needed for the stimulation of the muscle cell receptors

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and for the growth of the muscle tissue as previous studies confirm. This is why the muscle volume in people doing endurance exercise increases after a while (31). This result is compatible with the findings of a study by Keramer et al. (1992), about the effect of one session of endurance exercise on the free testosterone hormone (32).

Also, a study in women on the effects of one session of exercise with the intensity of 75% of maximum heart rate, lasting for 40 minutes revealed a significant increase in the testosterone level. The researchers explain the reason so that filtration of testosterone in the blood decreases as a result of endurance exercise, reduce hepatic blood plasma flow which results in a less filtration, and also because of a change in testosterone-binding proteins which increases the free testosterone level and reduces its consumption (33). But the insignificant decrease in the testosterone level in the low-intensity exercise experimental group in this research can be attributed to the increased FSH level in this group, which shows the positive effects of low-intensity exercises compared to the moderate-intensity exercises. On the other hand, it has been stated that exercise increases the beta-endorphin level, which in turn decreases GnRH and subsequently decreases LH level (34).

Conclusion

Based on the present research, it can be claimed that regular exercise particularly with low-intensity affects the improvement of the PCOS symptoms through its influence on sex hormones, especially the FSH and testosterone.

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Conflict of interests

Authors had no conflict of interests in this study.

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