

To determine the role of Home-based Aerobic Exercise Program on Serum High-sensitivity C-Reactive Protein (Hs-CRP) and Insulin Resistance in Polycystic Ovary women

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ABSTRACT

Aim: the aim of this study to determine the role of Home-based Aerobic Exercise Program on Serum High-sensitivity C-Reactive Protein (Hs-CRP) and Insulin Resistance in Polycystic Ovary women.

Methods: This quasi-experimental study was carried out on the study population consisting of female patients diagnosed with PCOS. According to the criteria, two of three items namely oligo-and/or anovulation, clinical and/or biochemical signs of excess androgen, polycystic ovaries detected on ultrasound should be present to make the diagnosis of PCOS. A total of 34 patients were consecutively included into the study. The subjects were divided into experimental group (aerobic exercise group, 17 patients) and control group (no intervention, 17 cases). The experimental group participated in a daily aerobic exercise program. The participants were asked to perform the stepping program at home following the schedule every morning at 10 o'clock in the morning.

Results: Mean (\pm SD) fasting glucose and insulin levels at baseline in the experimental group decreased after 16-weeks of home-based aerobic exercise. However, in control group, no such decrease was observed. There was a significant decrease in hs-CRP (35.29% decrease from baseline) and HOMA-IR (41.18% decrease from baseline) in the experimental group after the aerobic exercise program. However, no significant change was observed in hs-CRP (2.9 % change from baseline) and HOMA-IR (5.88% change from baseline) in control group. Comparison of hs-CRP and insulin resistance index before and after high intensity interval training and control groups. Data are presented as mean (\pm standard deviation); HOMA-IR: Homeostatic model of assessment of insulin resistance; hs-CRP: high-sensitivity C-reactive protein.

Conclusion: A 16-week home-based aerobic exercise program led to decrease in HOMA-IR and hs-CRP in a sample of female patients with PCOS. Although the effect of aerobic exercises in PCOS need more studies, these findings confirm the effective role of aerobic exercises in decreasing inflammation and improving insulin sensitivity in these patients.

Keywords: Aerobic Exercise, Serum High-sensitivity C-Reactive Protein (Hs-CRP), Insulin Resistance, Polycystic Ovary women

Introduction

The polycystic ovary syndrome (PCOS) is the most common endocrine-metabolic disorder that affects nearly 10%–15% of the women of reproductive age.^{1,2} It is characterized by clinical and/or biochemical hyperandrogenism, ovarian dysfunction and/or polycystic morphology, which are some reliable clues to diagnosis.³ The syndrome is also associated with hyperinsulinemia, glucose intolerance, abnormal blood lipid levels and obesity, which constitute the metabolic syndrome.⁴ One-third to one-half of women with PCOS also have metabolic syndrome, and insulin resistance may be the pathogenic link between these two

syndromes.^{5,6} These traits are related with obesity, oxidative stress, increased cardiovascular disease (CVD) risk and low-grade chronic inflammation.⁷⁻¹¹

Women with PCOS are at risk for glucose intolerance, type 2 diabetes and gestational diabetes mellitus (DM)², owing to abnormalities in insulin secretion and action.^{12,13} In addition, lower insulin sensitivity is observed in 30%–40% of women with PCOS, similar to the patients with type 2 diabetes¹⁴ and patients who develop glucose intolerance have a relative decrease in insulin secretion as well.¹⁵

Serum high sensitivity C-reactive protein (hs-CRP), a marker of low-grade chronic inflammation, is shown in multiple prospective epidemiological studies to predict incidence of CVD and seems to be as a potent predictor of cardiovascular events.¹⁶ The hs-CRP is closely linked to metabolic syndrome features, such as insulin resistance, abdominal obesity and dyslipidemia, and a large number of studies showed that serum CRP levels are significantly higher in patients with PCOS compared with healthy subjects.¹⁷ Some studies reported that high CRP levels are related to metabolic and endocrine abnormalities of patients with PCOS, while another study suggested that obesity plays the important role. However, CRP in lean patients with PCOS has not been fully evaluated and few data are available.

Thus, in view of the role attributed to inflammation in PCOS pathogenesis and the results of the previous studies, further studies are required to investigate the efficacy of exercise on inflammatory markers in these patients. The objective of the current study was to study the effects of a 16-week home-based aerobic exercise program on serum hs-CRP level and insulin resistance among PCOS patients.

Material and methods

This quasi-experimental study was carried out after taking the approval of the protocol review committee and institutional ethics committee. The study population consisted of female patients diagnosed with PCOS. According to the criteria, two of three items namely oligo-and/or anovulation, clinical and/or biochemical signs of excess androgen, polycystic ovaries detected on ultrasound should be present to make the diagnosis of PCOS.

Inclusion criteria

- Females with PCOS aged 18 to 38 years

Exclusion criteria

- Women with inability to perform physical exercise
- Cigarette smoking,
- Infection and taking any medication

Methodology

A total of 34 patients were consecutively included into the study. The subjects were divided into experimental group (aerobic exercise group, 17 patients) and control group (no intervention, 17 cases).

Aerobic Exercise Program

The experimental group participated in a daily aerobic exercise program. The participants were asked to perform the stepping program at home following the schedule every morning at 10 o'clock in the morning. To guide the participants, an audio file was prepared and delivered to the experimental group subjects via cell phone which contained 90 acoustic signals per minute for a four-stroke stepping and a rhythm of 25 steps per minute. The goal of the exercise program was to achieve the specific Exercise Energy Expenditure (ExEE) at each session. ExEE is amount of energy required by an individual to perform exercise. Specific

ExEE during the first four weeks of the exercise program was equivalent to 4% of the estimated individual energy needed to maintain weight, which during the fifth to the eight weeks of the exercise increased to 6%, and during the weeks 9 to 12 increased to 8%, and during the weeks 13 to 16 increased by 10%. After determining the required time for stepping for each individual, a table was designed which included schedule of stepping for the study period.

Laboratory parameter

Blood samples were taken two times to measure fasting glucose, fasting insulin, and hs-CRP. The blood samples were taken in certain hours of day to ensure that diurnal variations do not affect blood insulin and hs-CRP levels. The blood samples were centrifuged for 15 minutes (3000 rpm) for plasma separation and were frozen and kept at -80°C . Insulin level was measured using Sandwich ELISA. The participants were weighted using Seca Digital Weigh with 0.1-kg precision. The subject's height was measured by using measurement tape fixed on the wall with minimum 0.1 centimetres. The Body mass index (BMI) was calculated as body weight in Kg divided by height in metres squared.

Statistical analysis

To study the changes of hs-CRP and HOMA-IR index before and after the study, the paired t-test was used. To determine the differences of hs-CR and HOMA-IR index between the experimental and control groups, the independent t-test was used. The significance level was set at 0.05. All analyses were performed by SPSS software (25.0, IBM, US).

RESULTS

As observed, no significant difference was detected regarding age, height, weight, and BMI between the two groups.

Table 1. Demographic Profile of the patients

Parameter	Experimental group	Control group	p-value
Age (year)	32.64 (± 3.28)	29.31 (± 3.52)	0.41
Height (cm)	175.38 (± 3.19)	178.22 (± 6.46)	0.65
Weight (kg)	65.17 (± 4.67)	65.67 (± 6.39)	0.32
BMI (kg/m ²)	20.71 (± 1.66)	21.96 (± 2.19)	0.57

Mean (\pm SD) fasting glucose and insulin levels at baseline in the experimental group decreased after 16-weeks of home-based aerobic exercise. However, in control group, no such decrease was observed. There was a significant decrease in hs-CRP (35.29% decrease from baseline) and HOMA-IR (41.18% decrease from baseline) in the experimental group after the aerobic exercise program. However, no significant change was observed in hs-CRP (2.9 % change from baseline) and HOMA-IR (5.88% change from baseline) in control group.

Table 2: Comparison of hs-CRP and insulin resistance index before and after high intensity interval training and control groups. *Statistically significant p-value

		Baseline	After 16 weeks	p-value
Experimental group	Fasting glucose, mmol/L	5.16 (± 0.87)	4.46 (± 1.23)	<0.001*
	Fasting insulin, $\mu\text{IU/mL}$	14.22 (± 7.14)	10.36 (± 7.76)	0.007*
	HOMA-IR	3.34 (± 1.3)	1.95 (± 0.27)	0.03*
	hs-CRP, mg/L	6.51 (± 2.44)	4.02 (± 1.39)	0.003*
	Fasting glucose, mmol/L	5.22 (± 0.69)	5.33 (± 1.13)	0.11

Control group	Fasting insulin, $\mu\text{IU/mL}$	13.87 (± 8.42)	14.42 (± 8.12)	0.26
	HOMA-IR	3.26 (± 1.01)	3.44 (± 1.29)	0.18
	hs-CRP, mg/L	7.69 (± 2.74)	7.24 (± 2.18)	0.12

Data are presented as mean (\pm standard deviation); HOMA-IR: Homeostatic model of assessment of insulin resistance; hs-CRP: high-sensitivity C-reactive protein.

DISCUSSION

The findings showed that the aerobic exercise program had significant effect on decreasing hs-CRP and insulin resistance index among PCOS females. However, no significant difference was found in control group who did not receive any intervention. Thus, improvement in insulin resistance index in the experimental group could be attributed to the aerobic exercise program implemented in this group. Studies on the role of physical exercise in PCOS patients have not been done sufficiently. Vizza L et al., investigated the effect of Progressive Resistance Training (PRT) in PCOS women and reported mean hs-CRP level at baseline as 8.9 mg/L which decreased to 8 mg/dL after 12 weeks of PRT which statistically was not significant ($p=0.38$).¹⁸ The authors also investigated HOMA-2 which decreased from 2.62 to 2.56, a small non-significant decrease. This discrepancy can be related to the nature of the PRT which is different from aerobic exercise. Strenuous exercise may in fact cause a short-term increase in CRP but chronic habitual physical activity decrease CRP levels.¹⁹ In the present study, calorie intake and diet of the patients were not studied.

Insulin resistance is a pathologic situation in which, the normal amount of blood insulin is unable to provide a normal biologic response. In fact, insulin signalling is impaired. This decreased response could affect the entire metabolic effects of insulin.²⁰ As 70-80% of the uptake of circulating glucose is done by the muscles, this tissue has specific importance in insulin resistance development.²¹ Glucose absorption in target tissues is carried out by Glucose Transporter 4 (GLUT4). By activating phosphoinositide kinase, insulin changes phosphatidylinositol 4,5-bisphosphate to phosphatidylinositol (3,4,5)-triphosphate and activates other cytosol mediators such as PDK1 (phosphoinositide-dependent kinase-1), AS160 protein, GTPase, protein kinase B, protein kinases C.²² The findings of the current study showed that aerobic exercise improved insulin resistance in PCOS patients reflected by significant decrease in HOMA-IR after 16 weeks.

Aerobic exercise help in physiologic compatibility such as increasing oxidation enzymes, lowering fat tissues, reducing inflammatory markers such as hs-CRP²³, increasing anabolic hormones such as dihydrotestosterone²⁴, increasing capillary density, increase in the number of mitochondria, improving maximum oxygen intake and efficiency of cardiovascular system.²⁵ Increase in resistin level occurs following physical exercise and acts as an antioxidant.²⁶ Resistin acts as a pre-inflammatory mediator and stimulates release of tumour necrosis factor-alpha, monocyte chemoattractant protein-1 and endothelial adhesion molecules.²⁷

Regular physical activities could improve glucose tolerance in individuals; however, people do not have sufficient time to spend on sports.²⁸ Aerobic exercises affect fat tissues and stimulate muscular peroxisome Proliferator-activated receptor Gamma Coactivator 1-alpha (PGC-1 α), which increases fat oxidative capability and capacity. By aerobic exercise, perhaps the systemic inflammation reduces and insulin function increases; followed by reducing insulin resistance index in subjects; and ultimately, due to increase in tissues reactions towards insulin, the insulin amount of serum is consequently reduced.²⁹ Physical exercise improves insulin resistance via increase in transfer of glucose transporter (GLUT4) in cell membrane via activating intra-cellular messages after muscle contractions, increase in activity of glycogen synthase insulin and protein kinase B receptors, and trans-regulation of components engaged in insulin signalling flow.³⁰

In addition, the results of the research showed that the aerobic exercises resulted in significant differences between hs-CRP of PCOS patients. However, no significant changes were observed in control group. This improvement in hs-CRP level in experimental group could be attributed to the aerobic exercise. CRP activates the classic complement pathway and, similar to antibodies, causes opsonization, phagocytosis and lysis of invading organisms. It has been an accepted claim in the past decade that inflammatory mechanism plays a key role in the pathologic process of PCOS. It has been well established that PCOS patients show mild chronic inflammatory symptoms. In fact, these findings support the idea that there is a close relation between mild chronic inflammation and high levels of metabolic indices in PCOS women.³¹ Weight loss in women has been shown to prevent increase in the inflammatory cytokines and improvement of endothelial disorders.³⁰ Therefore, it seems that weight loss is one of the main mechanisms in CRP reduction.³² Due to direct relationship between CRP production with IL-6, serum IL-6 level should also decrease.³² Some researchers have introduced IL-6 as an inducing factor of insulin excretion in pancreatic beta cells. Constant engagement in intensive interval activities reduces fat. Since fat tissue is one of the major sources in IL-6 production. By lowering fat tissue, the serum level of this cytokine decreases as well. The reduction of serum IL-6 level weakens the signalling path of CRP and insulin production.³²

Conclusion

A 16-week home-based aerobic exercise program led to decrease in HOMA-IR and hs-CRP in a sample of female patients with PCOS. Although the effect of aerobic exercises in PCOS need more studies, these findings confirm the effective role of aerobic exercises in decreasing inflammation and improving insulin sensitivity in these patients.

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