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THE EFFECT OF HIGH INTENSITY INTERVAL TRAINING (HIT) ON INSULIN RESISTANCE AMONG WOMEN WITH POLYCYSTIC OVARIAN SYNDROME

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Abstract
Background: A few randomized trials assessed the effects of high intensity interval training (HIT) on insulin resistance among women with polycystic ovarian syndrome (PCOS). We now hypothesize that insulin resistance might be improved after HIT. Hence, the present study aimed to assess the effects of HIT on insulin resistance in Iranian PCOS patients.
Methods: This quasi-experimental study was performed on 25 women with the final diagnosis of PCOS according to the Rotterdam criteria. Fasting blood samples were taken from all patients to assess fasting glucose and insulin levels at the reference laboratory. After initial clinical and laboratory assessments, all patients were scheduled under the supervision of physical therapist for HIT as one-hour sessions once a week using treadmill aimed to achieve 85-75% of individual maximum heart rate (HRmax) for three months. After the completion of study protocol, the patients were reassessed.
Results: According to the definitive criteria of insulin resistance, 100% of subjects suffered insulin resistance at baseline. After the completing HIT program, significantly reduce in glucose and insulin parameters as well as increase in glucose to insulin ratio after HIT were found compared to the baseline values ($p < 0.001$ for all). Also, the overall prevalence of insulin resistance decreased from 100% to 52.0% with a significant difference ($p < 0.001$). The change in the parameters of serum insulin level, fasting glucose level and fasting glucose to insulin ratio were independent to anthropometric indices as well as to patients' age.
Conclusion: the use of HIT results in improvement of insulin resistance among PCOS women regardless of patients' baseline characteristics including age and BMI

Key words: *HIT, PCOS, insulin resistance, HRmax.*

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INTRODUCTION:

The main pathophysiological feature of polycystic ovarian syndrome (PCOS) is alteration in the hypothalamic-pituitary-ovarian axis leading inappropriate gonadotropin secretion and ovarian dysfunction [1]. The diagnostic criteria for PCOS should include two of the following three criteria: chronic anovulation, hyperandrogenism (clinical/biologic), and polycystic ovaries [2]. Along with sexual hormonal axis deviation, some metabolic disturbances have been shown to be linked with PCOS and thus the assessment of metabolic diagnostic markers to determine PCOS metabolic causes or to rule out differential diagnoses of the disease is essential [3]. Recent studies have suggested the significant association between PCOS and some comorbidities such as infertility, metabolic syndrome, type 2 diabetes, and cardiovascular risk factors. In this regard, some baseline screening laboratory studies including thyroid function tests, assessing lipid profiles, the measurement of serum cortisol concentration, and assessment of serum insulin like growth factor (IGF)–1 level are now recommended [4]. More important, the association between PCOS and insulin resistance and also insulin secretion defect has been also demonstrated [5]. Some mechanisms of the association between PCOS and insulin abnormalities include higher prevalence of obesity in PCOS and excessive expression of serine phosphorylation of the insulin receptor that can modulate the activity of the key regulatory enzyme of androgen biosynthesis or P450c17 [6]. Higher prevalence of insulin resistance in such patients along with lipid abnormalities can predict PCOS patients to cardiovascular diseases [7]. Moreover, the role of lipotoxicity in the development of androgen overproduction, in addition to its known role ininsulin resistance has been also described. Additionally, the role of weight gain and obesity in the development of PCOS is mediated at least in part, through worsening of insulin resistance [8]. Compensatory hyperinsulinaemia that develops in this context disrupts ovarian function, with enhanced androgen production and arrest of ovarian follicular development. Insulin resistance also contributes to the strong association of PCOS with adverse metabolic risk, including hyperglycemia, dyslipidemia and fatty liver [9]. Conversely, modest weight loss of just 5% body weight with improvement in insulin sensitivity, frequently results in clinically meaningful improvements in hyperandrogenic, reproductive and metabolic features [10].Thus, it seems that physical activity through losing weight may improve insulin resistance in PCOS patients. It has been revealed that the progressive resistance training has positive effects on the hormonal and physical characteristics of women with PCOS and controls [11]. Also, some evidences are available in beneficial effects of high intensity interval training (HIT) and strength training on metabolic, cardiovascular and hormonal outcomes. It has been demonstrated that HIThas greater impact on insulin resistance than moderate continuous training [12,13].

To our knowledge, a few randomized trialsassessed the effects of HIT on insulin resistance among women with PCOS. We now hypothesize that insulin resistance might be improved after HIT. Hence, the present study aimed to assess the effects of HIT on insulin resistance in Iranian PCOS patients.

METHODS:

This quasi-experimental study was performed on 25 women aged 18 to 35 years who referred to infertility department at Mahdieh hospital in Tehran, Iran between September 2014 and July 2015. The inclusion criterion was the final diagnosis of PCOS according to the Rotterdam criteria [14] as existence of two of the following three criteria: oligo- and/or anovulation, clinical and/or biochemical hyperandrogenism, and polycystic ovaries on ultrasound. Cut-off values for biochemical hyperandrogensim was defined as testosterone >3.0 nmol/L, calculated free testosterone > 32 nmmol/L, SHBG <30 nmol/L, or free androgen index (FAI as 100 x testosterone concentration (nmol/L) /SHBG concentration (nmol/L) >5% [15]. Oligomenorrhea was defined as an intermenstrual interval > 35 days and < 8 menstrual bleedings in the past year. Amenorrhea was defined as absent menstrual bleeding or none bleeding in the past 90 days. Some of the included women were diagnosed by their own gynecologist. The exclusion criteria were history of diabetes mellitus, hypertension, cardiovascular disorder, thrombosis or seizure, receiving antiglycemic or antilipidemic medications within 6 months ago, pregnancy, receiving especial dietary regimen before entering the study, inability to complete the treatment course, or intolerance of extreme sports activities for medical reasons. All subjects were interviewed for collecting baseline characteristics and medical history and entered into the study checklist. The anthropometric parameters including body weight, height, waist circumference and also waist to hip circumferences ratio were measured. Fasting blood samples were taken from all patients to assess fasting glucose and insulin levels at the reference laboratory. After initial clinical and laboratory assessments, all patients were scheduled under the supervision of physical therapist for HIT as one-hour sessions once a week using treadmill aimed

to achieve 85-75% of individual maximum heart rate (HRmax) for three months. After the completion of study protocol, the patients were reassessed by the gynecologist and laboratory parameters were retested. The study endpoint was to assess the effect of HIT on reducing insulin resistance.

Results were reported as mean ± SD for the quantitative variables and percentages for the categorical variables. The groups were compared using the Student's t-test for the continuous variables and the chi-square test (or Fisher's exact test if required) for the categorical variables. Changes in study parameters after intervention were determined by dividing the change between the baseline and final measurements by the duration of follow-up. P values of 0.05 or less were considered statistically significant. All the statistical analyses were performed using SPSS version 16.0 (SPSS Inc., Chicago, IL, USA) for Windows.

RESULTS:

In total, 25 women were completed the trial. The mean age of participants was 30.1 ± 3.7 years ranged 24 to 37 years. The mean body weight was 81.3 ± 15.7 kg, the mean height was 160.7 ± 5.7 cm and the mean body mass index was 30.1 ± 3.7 kg/m^2 ranged 25 to 39 kg/m^2. The baseline value of serum insulin was 28.7 ± 4.7 microIU/mL ranged 22 to 40 microIU/mL, the mean serum glucose level was 102.8 ± 8.6 mg/dl ranged 90 to 119 mg/dl, and the mean fasting glucose to insulin ratio was also 3.7 ± 0.4 ranged 2.76 to 4.27. According to the definitive criteria of insulin resistance, 100% of subjects suffered insulin resistance. After the completing HIT program, the mean serum insulin level reached to 21.1 ± 3.5 microIU/mL, the mean glucose level reached to 93.8 ± 5.3 mg/dl, and the mean fasting glucose to insulin ratio reached to 4.5 ± 0.6 indicating significantly reduce in glucose and insulin parameters as well as increase in glucose to insulin ratio after HIT compared to the baseline values ($p < 0.001$ for all). Also, the overall prevalence of insulin resistance decreased from 100% to 52.0% with a significant difference ($p < 0.001$). As shown in Table 1, the change in the parameters of serum insulin level, fasting glucose level and fasting glucose to insulin ratio were independent to patients' anthropometric indices that the significant change in all parameters significantly occurred in both patients with BMI < 30 kg/m^2 (n = 13) and those with BMI ≥ 30 kg/m^2 (n = 12). Similarly, by adjustment for patients' age, decreasing trend in serum insulin level and fasting glucose level and also increase in fasting glucose to insulin ratio after HIT was observed in the three age subgroups of less than 27 years, 27 to 30 years, and more than 30 years (Table 2).

Table 1: The change in metabolic parameters after HIT adjusted for body mass index

Parameter	Before HIT	After HIT	P-value
BMI > 30 kg/m^2			
Insulin	27.7 ± 4.9	20.8 ± 3.5	< 0.001
Glucose	100.4 ± 7.7	93.7 ± 6.4	< 0.001
Insulin to glucose ratio	3.7 ± 0.5	4.6 ± 0.6	< 0.001
BMI ≥ 30 kg/m^2			
Insulin	29.7 ± 4.5	21.5 ± 3.6	< 0.001
Glucose	105.4 ± 9.1	93.9 ± 4.1	< 0.001
Insulin to glucose ratio	3.6 ± 0.3	4.5 0.6	0.001

Table 2: The change in metabolic parameters after HIT adjusted for patients' age

Parameter	Before HIT	After HIT	P-value
Age < 27 years			
Insulin	29.1 ± 6.4	21.8 ± 4.3	0.004
Glucose	103.0 ± 9.8	96.1 ± 6.1	0.010
Insulin to glucose ratio	3.6 ± 0.5	4.5 ± 0.8	0.020
Age 27 to 30 years			
Insulin	27.5 ± 3.1	20.4 ± 4.4	< 0.001
Glucose	103.0 ± 9.8	92.2 ± 5.9	< 0.001
Insulin to glucose ratio	3.6 ± 0.3	4.6 ± 0.7	0.001
Age > 30 years			
Insulin	29.4 ± 5.1	21.4 ± 1.9	< 0.001
Glucose	105.3 ± 9.1	93.9 ± 4.1	0.001
Insulin to glucose ratio	3.6 ± 0.4	4.4 ± 0.4	0.001

DISCUSSION:

Reviewing the literature showed only one clinical trial on effects of HIT on metabolic parameters including insulin resistance among those women with PCOS. In the study by Almenning et al [16], HOMA-IR improved significantly only after HIT. In their study, not only insulin resistance significantly reduced, high-density lipoprotein cholesterol increased, endothelial function, measured as flow-mediated dilatation of the brachial artery increased significantly, and fat percentage decreased significantly after HIT even without changes in body weight. In fact, programing HIT improved insulin resistance and other metabolic indicators even without exercise-induced weight loss. In our study and similar to the pointed study, we showed considerable reduce in both serum glucose and insulin levels independent to patients' age and BMI. In fact, the improvement in metabolic biomarkers after HIT can be achieved even independent to advanced age and patients' obesity. However, in Almenning et al survey [16], the change in insulin level occurred without any change in serum glucose level. Previous studies emphasized more on the effects of moderate intensity training on metabolic status, but we could show that employing HIT achieve more improvement in insulin resistance and glucose level without increasing the risk for heavy exercise-induced complications. In other words, previous randomized controlled trials on the isolated effect on IR after endurance training in women with PCOS have been using moderate intensity [17–19]. Some others could demonstrate benefits of the combination of moderate intensity exercise and dietary intervention/advice [20,21]. It can be argued based on our trial that HIT can induce insulin resistance decrease as sole intervention regardless of other interventions and baseline variables. In fact, it seems that using HIT compared to moderate intensity training, more improvement in insulin resistance is expected [22].

The improvement of insulin resistance following HIT can be explained by some signaling pathways. It can be first due to the significant change in body fat percentage and amount of visceral fat that was also observed in Almenning et al survey [23], however some other studies could not demonstrate the change in body fat percentages after HIT [19] and thus it should be more assessed in further studies. It might be also induced by some genetic susceptibility explaining the conflicting results of the studies.

CONCLUSION:

In final, the use of HIT results in improvement of insulin resistance among PCOS women regardless of patients' baseline characteristics including age and BMI. This phenomenon may be affected by the influence of HIT on visceral fat mass and also body composition; however there are some conflicting results on this association requiring further experiments.

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