Effects of aerobic Training on clinical symptoms and biochemical parameters in Women with Polycystic Ovarian Syndrome

Mohammad Reza Kordi , Zahra Motie , Ramin Amirsasan , Amir Letafatkar

Abstract
Objective: The aim of this study was to evaluate the effects of aerobic training on clinical symptoms and biochemical parameters in PCOS women.

Methods: Twenty four PCOS women’s with mean Age 22.7± 3.77 years old, Body Height 159.87± 5.29 Cm, Body Weight 69.88± 14.12 Kg and BMI 27.53± 5.02 were randomly selected and subdivided into two groups, each composed of 12 subjects. Clinical data (ovarian morphology, BF%, WC, WHR) and serum hormone levels (insulin, Androstenedione, testosterone, DHEA-S and SHBG) were evaluated at baseline and after 12 week. A paired t-test and other data’s analyzed by sample t-test (α ≤ 0.05) was used in determining statistical significance using the SPSS program for Windows, version 16.0.

Results: After 12 weeks training, PCOS-T showed a significant reduction in ovarian size, BF%, WC, WHR. Fasting insulin, androtestenedione hormone significantly reduced in PCOS- T. Serum testosterone, DHEA-S and SHBG levels uncharged in PCOS- T. no changes were observed in PCOS- Un T.

Discussion and conclusion: The probable mechanism that thorough them aerobic exercise did affect ovarian size could be included: emerging endocrine environment follow the SHBG increasing, free androgen decreasing and improvement in insulin sensitivity. The ovarian size changes in PCOS women probably result in circulating androtestenedione decreasing and this can improve clinical symptoms and biochemical parameters. We recommended that with precise and further studies, the aerobic exercises may be useful for women’s with PCOS.

1. Introduction
Polycystic Ovarian Syndrome (PCOS) is common condition in women that wreaks havoc on hormones and causes physical and psychological damage. Polycystic ovarian syndrome (PCOS) is a complex hormonal disturbance that affects the entire body and has numerous implications for general health. Women with this syndrome have, over the course of their life, an increased risk of coronary disease, diabetes and endometrial cancer [1,2,3]. The disorder is probably the most common hormonal abnormality in women of reproductive age and certainly is a leading cause of infertility. There are three broad reasons why PCOS patients seek medical care: 1) menstrual cycle disturbance and infertility 2) problems of appearance and self esteem arising from obesity and excessive hair growth, and 3) metabolic derangements, including abnormalities in blood fat (lipid) levels, insulin/glucose (sugar), and elevated blood pressure (hypertension) [4,5,6,7].

PCOS is the first cause of infertility in women, but it also should be considered a multifaceted disease [8,9]. Chronic Anovulation, Hyperandrogenism, and insulin resistance (IR) are its main characteristics [10]. IR, a well-recognized cardiovascular risk (CVR) factor [8,9,10,11,12], is frequently associated with other CVR factors (e.g. dyslipidemia, hypertension, glucose intolerance, and diabetes) [13,14,15], thus increasing CVR profile in young PCOS women[16].

Treatment of PCOS is focused on both normalizing short term signs of Hyperandrogenism and anovulation and reducing metabolic complications [18]. Diet and exercise are recommended as first-line treatment of oligomenorrhea, hirsutism, infertility and obesity in PCOS by the majority of endocrinologists and gynecologists [17,18,19].
In PCOS women, short-term weight-loss intervention studies have decreased abdominal fat [20,21], Hyperandrogenemia [20], and improved insulin sensitivity [20,21] and lipid profile [21]. In non-PCOS subjects, lifestyle modification has also proved as efficacious as pharmacological intervention in reducing the risk of developing type 2 diabetes mellitus [22].

The National Institutes of Health clinical guidelines for the long-term treatment of overweight and obesity emphasize the importance of achievable and sustainable goals, notably a combination of diet modification, physical activity, and behavior therapy [23]. In PCOS women, we recently documented an impaired cardiopulmonary functional capacity strictly related to IR [14]. In women with proven to PCOS, it seems proven to impaired clinical symptoms and biochemical parameters. There are some intriguing reports showing higher clinical symptoms and biochemical parameters even at an early age [9,10]. Some studies given the recognized beneficial effects of exercise training (ET) on oligomenorrhea, hirsutism, infertility, and obesity in PCOS women [19], this study was performed to establish whether these beneficial effects may be extended to improve the clinical symptoms and biochemical parameters in young PCOS women.

2. Method and materials

2.1. Patients: twenty four young overweight Polycystic Ovarian Syndrome Women’s (PCOS) were enrolled. Polycystic ovaries were identified by transvaginal ultrasonography examination [24,25,26].

For this study executing, 24 PCOS women with mean Age 22.7 ± 3.77 years old, Body Height 159.87 ± 5.29 Cm, Body Weight 69.88 ± 14.12 Kg and BMI 27.53 ± 5.02 were randomly selected and subdivided into two groups, each composed of 12 subjects. Clinical data (ovarian morphology, BF%, WC, WHR) and serum hormone levels (insulin, Androstenedione, testosterone, DHEA-S and SHBG) were evaluated at baseline and after 12 week.

Exclusion criteria included pregnancy, glucose intolerance (as screened by a 2-h oral glucose tolerance test) and diabetes, hypothyroidism, hyperprolactinemia, Cushing’s syndrome, nonclassical congenital adrenal hyperplasia, and use of oral contraceptives, glucocorticoids, antiandrogens, ovulation induction agents, antiandrogen or antiobesity drugs, or other hormonal drugs within the previous 6 months. Subjects with neoplastic, hepatic, respiratory, and any cardiovascular disorder or other concurrent medical illness (i.e. heart failure, lung or renal disease) were also excluded from the study. None of the study patients drank alcoholic beverages.

2.2. Protocol

The study was conducted according to the guidelines of the Declaration of Helsinki, and the institutional ethical committee approved the study protocol. The purpose of the protocol was explained to each subject, and written informed consent was obtained from each patient before beginning the study. A common core of assessments was performed at baseline and after 3 months. All patients underwent blood sampling for a hormonal assessment, lipid profile, and fasting glucose and insulin levels.

During the same visit, all subjects underwent cardiovascular and endocrinological examination, 12-lead electrocardiography, transvaginal ultrasonography, aerobic exercise test, anthropometric measurements, including height, weight, body mass index (BMI), waist circumference (WC), waist/hip ratio (WHR) and leisure-time physical activity (LTPA) questionnaire [27] as detailed below. At study entry, general dietary and behavioral advice without a structured caloric restriction program was given to the entire PCOS study population. All of the PCOS population was counseled to achieve a healthy balanced meal plan with regular food with a nutritional composition of 50% of calories from carbohydrate, 25% from protein, and 25% from fat. Intake of low glycemic index foods was encouraged. At study entry, PCOS women were randomly subdivided into two groups composed of 12 patients each; the PCOS-T (trained) group underwent a 3-month structured ET program, whereas the PCOS-UnT (untrained) group did not. None of the subjects received any medications throughout the study. All clinical assessments were performed by the same physician who was blinded to the patient allocation into the study protocol. All study procedures were completed under the same conditions, and at the same time of day for both the baseline and follow-up tests.

In this study, Harpenden caliper (with precision 0.2 Mm), polar beat (Model T31, N2965), centriuge machine (Hettich Model), Chemiluminescence (Model Liaisan insulin– 310360), ELISA machine (Model Awareness star fax), sonography scan machine (Model GE-logic 500) measurement of photo absorption in variables such as [Androstenedione, Testosterone, SHBG, DHEA-S, Prolactin, TSH and 17hydroxy progesterone], Nautilus Ergometer, 24 H diet and LTPA questionnaire used respectively for skin fold measurement, heart rate controlling, serum isolation, insulin measurement, measurement of Ovarian bulk, measurement of 02 consumption, for recording subjects 24 H regimen and medical history. Training intensity measured via carvonen method.

2.3. Biochemical assays

All blood samples were obtained in the morning between 8 and 9 h after an overnight fasting during the early follicular phase (d 2–4) of progesterone-induced menstrual cycle. Blood samples were collected into tubes containing EDTA after a 30-min resting period in the supine position. All blood samples were immediately centrifuged at 4 C for 20 min at 1600 g and stored at 20 C until assayed. Plasma LH, FSH, prolactin, estradiol, progesterone, 17-hydroxyprogesterone, testosterone, androstenedione, and dehydroepiandrosterone sulfate levels were measured by specific RIAs as previously described [15,16]. The levels of SHBG were measured using an Immunoradiometric assay, and the free androgen index was calculated [testosterone (nmol/liter)/SHBG (nmol/liter) ×100]. Blood insulin and glucose levels were measured by a solid-phase chemiluminescent enzyme immunoassay and the glucose oxidase method, respectively [15,16].

2.4. LTPA questionnaire

The self-reported LTPA, including all recreational activities, housework, and yard work (e.g. sweeping, shopping, gardening, walking, different types of sports, etc.) was recorded. Using a
standardized classification of the energy expenditure associated with physical activities [27,28,29], we calculated a weekly energy expenditure score (total LTPA level) in metabolic equivalents per hour per week (METs-h/wk). LTPA level was graded into four categories of increasing order with the aid of the following scheme: 1) no weekly LTPA; 2) only light LTPA most of the week; 3) strenuous LTPA (large increase in heart rate, breathing, and perspiration) for at least 20 min once or twice a week; and 4) strenuous LTPA for at least 20 min three times a week or more. To simplify this gradation, we shortened the description into no, low, moderate, and high LTPA. Occupational physical activity was not included in the analysis because of the subjectivity of the questions and its different nature compared with the question about physical activity at home. Finally, participants were asked to estimate the number of hours per day they spent engaged in sedentary behavior, including time spent sitting as well as lying down or sleeping.

2.5. Aerobic exercise program

All patients underwent an incremental aerobic exercise test on a bicycle ergometer. The PCOS-T group underwent a 3-month aerobic exercise program on a hospital ambulatory-based regimen. Training sessions, performed three times per week under continuous electrocardiographic monitoring, were supervised by a cardiologist, a physiotherapist, and a graduate nurse. Each session was preceded by a 5-min warm-up and followed by a 5-min cool-down. Exercise was performed for 30 min on a bicycle ergometer with the target of 65–70% of the maximal oxygen consumption (VO2max) achieved at the initial aerobic exercise test monitored by a wearable device. Exercise workload was gradually increased until the achievement of the predefined target.

2.6. Statistical analysis

For categorical variables the chi square test was performed. For two related categorical variables, the McNemar-Bowker test of symmetry was used. The pre and post-test data were analyzed with a paired t-test and other data’s analyzed by sample t-test. An alpha level of (0.05) was used in determining statistical significance using the SPSS program for Windows, version 16.0.

3. Results

There were no significant differences between the two groups in baseline clinical symptoms and biochemical parameters. All PCOS patients showed polycystic ovaries and anovulation. Fifteen patients had clinical Hyper androgenism, and 12 showed biochemical Hyperandrogenism.

All subjects completed the study protocol. No adverse events took place during any of the training sessions. In PCOS-T, the average exercise intensity was 62± 1.4% of initial VO2max, and averaged 97± 13 min per week of training session. Attendance was 100% in the PCOS-T group for the 3-month aerobic exercise program. After intervention, 9 of 12 women of the PCOS-T group showed normal menstrual cycles.

After a 3-month aerobic program, a significant improvement in VO2max (P<0.001), VO2AT (P<0.001), and Wattmax (P<0.001) was observed in PCOS-T compared with PCOS-UnT. A significant reduction in the slope of increase in ventilation over carbon dioxide output (VE/VCO2slope) (P<0.05), HRrest (P<0.001), SBPrest (P<0.01), and diastolic blood pressure at peak exercise (DBPpeak) (P<0.01) was also observed in PCOS-T compared with PCOS-UnT.

Table 1. Variables alteration during aerobic exercise period in experimental group.

<table>
<thead>
<tr>
<th>Statistics variables</th>
<th>Mean differences</th>
<th>t</th>
<th>df</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right ovarian</td>
<td>-2.72</td>
<td>-3.61</td>
<td></td>
<td>0.001*</td>
</tr>
<tr>
<td>Left ovarian</td>
<td>-3.73</td>
<td>-4.1</td>
<td></td>
<td>0.002*</td>
</tr>
<tr>
<td>Androtestenedione</td>
<td>-0.64</td>
<td>-2.77</td>
<td></td>
<td>0.001*</td>
</tr>
<tr>
<td>Testosterone</td>
<td>-0.64</td>
<td>-2.77</td>
<td></td>
<td>0.03</td>
</tr>
<tr>
<td>DHEA-S</td>
<td>-0.26</td>
<td>-1.44</td>
<td>22</td>
<td>0.16</td>
</tr>
<tr>
<td>SHBG</td>
<td>-2.30</td>
<td>-0.84</td>
<td></td>
<td>0.40</td>
</tr>
<tr>
<td>WHR</td>
<td>0.02</td>
<td>-2.65</td>
<td></td>
<td>0.001*</td>
</tr>
<tr>
<td>WC</td>
<td>-2.19</td>
<td>-4.22</td>
<td></td>
<td>0.002*</td>
</tr>
</tbody>
</table>

*there are significant changes.

Table 2. Baseline and 3 month LTPA level in PCOS_T and PCOS_UnT study population.

<table>
<thead>
<tr>
<th>Statistics variables</th>
<th>PCOS_T(n= 12)</th>
<th>Third month</th>
<th>PCOS_UnT(n= 12)</th>
<th>Third month</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>LTPA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>12</td>
<td>8</td>
<td>11</td>
<td>9</td>
<td>&lt;0.002 a</td>
</tr>
<tr>
<td>Low</td>
<td>5</td>
<td>4</td>
<td>7</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>4</td>
<td>5</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>3</td>
<td>7</td>
<td>3</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>61</td>
<td>13.4</td>
<td>6.2</td>
<td>5.9</td>
<td></td>
</tr>
<tr>
<td>LTPA level</td>
<td>± 3.7</td>
<td>± 3.1</td>
<td>±0.001</td>
<td>± 3.3</td>
<td>±7.5</td>
</tr>
<tr>
<td>(METs-h/wk)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.207 b</td>
</tr>
</tbody>
</table>

Data are n except where indicated otherwise.

*By McNemar-Bowker test.
†By the paired-samples t test.

4. Discussion

Considering the results of this study, conducted three months of aerobic training significantly reduced the volume of the ovaries. The result of this part of the research is in parallel with results of Hahn el al [9]. In this regard, moderate exercise can cause adjustment in sympathetic nerve update to ovaries, preventing the indiscriminate growth and reduce them to ovarian stroma. Mechanism, by which ovarian volume is reduced, is not known and is suspected of being the only factor likely to cause endocrine environment favorable looking to increase SHBG and free androgen reduction and improving insulin sensitivity. Reduction in ovarian volume may be due to a reduction in the ovarian stroma. Amount of ovarian stroma by producing excessive stroma Teka derived cells, especially linked Androtestenedione. In patients with a37x77 normal menstrual cycles.
with polycystic ovary syndrome, a reduction in ovarian volume can be reduced circulating Androstenedione and improves clinical symptoms in patients with polycystic ovary syndrome. However, certain comments in this area require further research.

According to the study, significant change was found in both fasting insulin and Androstenedione hormones. Overview of research conducted shows that most research on patients with polycystic ovary syndrome women has been made with obesity and overweight. This research have been considered compensatory the symptoms related to insulin resistance and hyper insulinenic and recommended weight loss of low-calorie diet or low calorie diet combined with physical activity in reducing waist circumference and abdominal fat in increasing insulin sensitivity and reduce Fasting insulin in causing menstrual and hormonal changes in the coefficients were effective.

Despite the presence of these clinical symptoms in PCOS women, there are no adequate prospective data documenting the effects of a structured aerobic program in PCOS women. The current prospective randomized study was designed for evaluating the effects of a structured aerobic ET program on clinical symptoms and biochemical parameters in a PCOS population with no exercising habit (no or low LTPA level). Thus, the increased LTPA level, the BMI and WC reduction and the improvement of IR may play a role conferring to the aerobic program a significant long-term prognostic advantage.

Based on this study results after 3-month ET, PCOS-T showed a significant reduction in ovarian volume, BF%, WC, WHR. Fasting insulin, Androstenedione hormone significantly reduced in PCOS-T. Serum testosterone, DHEA-S and SHBG levels unchanged in PCOS-T. After 3 month, no changes were observed in PCOS-Un T. Larger and older population of women with PCOS, and long-term follow-up studies are required to evaluate whether these findings may translate into long-term reduction of ovarian size. The probable mechanism that thorough them aerobic exercise did affect ovarian size could be included: emerging endocrine environment follow the SHBG increasing, free androgen decreasing and improvement in insulin sensitivity. The ovarian size changes in PCOS women probably result in circulatin Androstenedione decreasing and this can improve clinical symptoms and biochemical parameters. Skeletal muscle is the major site of insulin-mediated glucose disposal and is implicated in the pathogenesis of IR [30]. Some reports [1-9] suggest that insulin action may be related to the oxidative capacity of skeletal muscle. VO2max represents a validated index for assessing cardiovascular functional capacity [31]. The levels of physical activity and insulin sensitivity are positively correlated [6,9], and VO2max is considered a strong determinant of the insulin sensitivity index in both men and women [27]. The increased prevalence of IR in PCOS and its strong association with inactivity may lead to an exercise-deficient phenotype [12,14,16], manifested by a greater disruption both of skeletal and muscle cellular metabolism and also correlated to a chronic low-grade inflammatory state [30-34]. However, the decrease in body fatness with no weight reduction in trained obese PCOS women has to be interpreted in the absence of data regarding LTPA level, also taking into consideration the small sample size population [31]. In the present study, we demonstrate that a 3-month aerobic training induced a significant improvement in clinical symptoms, biochemical parameters and insulin sensitivity and also led to a significant reduction in BMI in the PCOS population, named PCOS-T. In our view, the significant BMI and WC reduction observed in our PCOS-T group represent the combined effect of the complete adherence to the aerobic training sessions and of the significant increase in LTPA level.

It is well known that exercise improves glucose homeostasis related to up-regulation of the expression and/or activity of proteins involved in insulin signal transduction in skeletal muscle [32]. Physical fitness is associated with an early onset of metabolic syndrome [33] and a reduced mortality [25].

In conclusion, a structured 3-month ET program improved cardiopulmonary functional capacity and physical fitness, insulin sensitivity, and BMI, and reduced clinical symptoms and biochemical parameters in PCOS women. Given the strong evidence for a direct role of physical activity in the prevention of IR and the fact that ET increases mitochondrial biogenesis and improves glucose tolerance and insulin action in IR subjects, the present work strengthens the recommendation to apply primary defense mechanisms such as exercise in young women with PCOS.

Conclusions:
Based on this study results, a 3-month aerobic exercise program improved in clinical symptoms and physical fitness, and reduced fasting insulin and serum Androstenedione in young PCOS women. We suggest that along with other medications, an aerobic exercise also could be used in women with polycystic ovary syndrome and patients that have similar characteristics with subjects of this study.

Acknowledgement
Gratitude is expressed to the subjects that participated in this study as well as to each of the assistants who were instrumental in the collection of the data. This study was funded by a product grant from the University of Tehran (Tehran, Iran). The researchers independently collected, analyzed and interpreted the results and have no financial interests in the results of this study. Also, dissemination of the results in this study does not constitute endorsement by the researchers or their institutional affiliations.

6. References


