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Effect of aerobic exercise on non-obese adolescent girls with polycystic ovarian syndrome

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Polycystic ovary syndrome (PCOS) is the most common endocrine disorder among reproductive-aged women and the main cause of infertility due to anovulation. The aim of the current study was to investigate the effect of aerobic exercise on non- obese adolescent girls with polycystic ovarian syndrome. Fifty non-obese adolescent girls diagnosed with PCOS participated in this study. Their ages were ranged from 15 to 19 years old, their BMI was from 18.5 to 24.9 kg/m², their LH/FSH ratio was >1.5. All girls experienced amenorrhea (no menses in the last 6 month) or oligomenorrhea (less than four cycles in the last 6 month) and typical ultrasonoghraphic presentation of PCOS of multiple subscapular ovarian follicles. They were divided randomly into 2 equal groups (A & B); Group A treated by metformin drug for 24 weeks, group B treated by metformin drug and performed moderate intensity aerobic exercise program for 45 minutes, three times per week for 24 weeks. Evaluation was carried out before and after 6 months of the treatment program. Results of this study revealed that; post treatment, there was a significant difference in FSH (more increase in group B), weight, BMI, LH, LH /FSH ratio, Total Testosterone, fasting blood glucose, fasting blood insulin and menstrual cycle interval (more decrease in group B), there is no significant difference in waist / hip ratio and fasting glucose /insulin ratio. It was concluded that Long-term regular exercise provides betters results in reproductive and metabolic parameters and improve menstrual irregularity in non-obese adolescent girls with PCOS and consequently improve the quality of life of these patients.

Keywords: Aerobic exercise; Non obese; Adolescent girls; Polycystic ovarian syndrome.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in adolescent and young women that have both reproductive and metabolic consequences. PCOS affects 5–10% of reproductive-aged women (Ehrmann, 2005). It is thought to be one of the leading causes of female subfertility (Goldenberg and Gluek, 2008).

Polycystic ovary syndrome is the most common cause of chronic hyperandrogenic anovulation and the single most common cause of infertility in young women (Rosenfield, 2015). It is also a risk factor for metabolic syndrome-related comorbidities and for impaired well-being and mortality (Doherty, 2015).

The Rotterdam 2004 Consensus Workshop proposed that PCOS is a syndrome of ovarian dysfunction, and recommended that two of the following criteria should be present to establish a diagnosis: chronic oligo- or anovulation for more than 6 months, clinical and/or biochemical evidence of hyperandrogenism, and polycystic ovaries on ultrasound.

The characteristic biochemical abnormalities are elevation of serum androgen concentrations (the most consistent endocrine abnormality) and luteinizing hormone (LH) concentrations, but with normal levels of follicle-stimulating hormone (FSH). Importantly, PCOS is also associated with metabolic abnormalities, central to which are insulin resistance and hyperinsulinaemia, which carry an increased risk of developing type 2 diabetes in later life (Franks, 1995).

At least 50–60% of PCOS patients are obese or overweight, and hyperinsulinaemia is the usual accompaniment in these women (Grulet and Hecarf, 1993). However, not all women with PCOS are obese. Between 20–30% of women with PCOS are normal weight or thin, and the pathophysiology of the disorder in these women may differ from that in obese women. It has been suggested that PCOS develops in non-obese women because of a hypothalamic-pituitary defect that results in increased release of LH, and that insulin plays no role in the disorder (Jacobs, 1995).

It was found that metabolic disorders and visceral fat accumulation are closely associated in non-obese patients with PCOS and suggested that visceral fat accumulation may be an early marker of metabolic disorders in non -obese patients with PCOS (Yildirim, 2003).

Treatment of PCOS must focus both on normalizing short-term signs of hyperandrogenism and anovulation and on reducing metabolic complications. This can be achieved through pharmacological intervention or preferably lifestyle modification. The most preferred and effective method of treatment of PCOS is lifestyle modification (Norman et al., 2002).

Incorporating moderate exercise training (ET) as a treatment for clinical complications in PCOS may be favorable, considering the beneficial effects of exercise in other insulin resistant population, independent of weight loss [(Hamdy et al., 2001) & (Bruce et al., 2004)].

Exercise improves ovulation rates and is potentially more beneficial than dietary restriction in restoring reproductive function. Enhanced insulin sensitivity underpins restoration of reproductive function through hormonal improvements, including reduced androgens. This improves the ovarian hormonal environment allowing maturation of follicles thereby restoring ovulation (Cheryce et al., 2011).

Exercise has shown to modulate insulin sensitivity and lipid metabolism in skeletal muscle. Exercise improves insulin sensitivity by increasing intra myocellular triacylglycerol concentration (Li et al. 2015). Improvement in insulin sensitivity could be due to more efficient lipid turnover resulting in increased muscle lipid uptake, transport, utilization, and oxidation. The literature states the efficacy of exercise training in combating metabolic syndrome in PCOS patients by marking improvements in apolipoprotein, adiponectin in the process of lipid turnover, and uptake in skeletal muscles (Hutchison et al., 2012).

MATERIALS AND METHODS

Subjects:

Fifty non-obese adolescent girls diagnosed with PCOS participated in this study. They were selected randomly from outpatient clinic of gynecology in Al Khazendara General Hospital in Cairo. The study was conducted through the period from July 2016 until December 2017. They were diagnosed by gynecologist. Their ages were ranged from 15 to 19 years old. Their BMI was from 18.5 to 24.9 kg/m². Their LH/FSH ratio was >1.5. All girls experienced amenorrhea (no menses in the last 6 month) or oligomenorrhea (less than four cycles in the last 6 month) and typical ultrasonoghraphic presentation of PCOS of multiple subscapular ovarian follicles. The following patients were excluded: patients with BMI > 25 kg/m² or their BMI< 18 kg/m², anemia, musculoskeletal or cardiovascular disorder, diabetes mellitus (DM), impaired glucose tolerance, or other hormonal dysfunctions (pituitary, thyroidal, or adrenal causes), history of any psychiatric condition, history of orthopedic or other physical symptoms that would otherwise limit exercise performance; and those who had exercised regularly within the last 6 months and smokers. The design of this study was two groups pre and post experimental study. Patients were divided randomly into two equal groups (A&B): Group A (Control group): 25 girls were treated by metformin drug at a dose of 500 mg orally twice daily, 20 min before lunch and dinner for 24 weeks. Group B (Study group): 25 girls were treated by metformin drug at a dose of 500 mg orally twice daily, 20 min before lunch and dinner and all of them performed moderate intensity aerobic exercise program for 45 minutes, three times per week for 24 weeks. Randomization was carried out using computer- generated random number table and pre-labeled, sealed envelope.

Ethical committee approval:

The study was approved by research ethical committee, faculty of physical therapy, Cairo

University (NO:).

II- Procedures:
All girls were given a whole demonstration of the protocol of the research and consent form was signed for each girl before participating in the study.

A) Evaluative procedures:

1-History taking:
A detailed medical and gynecological history was taken from each girl in both groups (A&B) before treatment. The dates of menstrual cycles 6 months before intervention and during treatment were recorded using Menstrual Record Chart.

2-Body Mass Index (BMI):
Weight and height were measured for each girl in both groups (A&B) before and after the treatment according to the following equation:
BMI=weight/height^2 (Kg/m^2).

3-Hip and waist circumference measurement:
Hip and waist circumference were determined using a tape measure, measuring waist circumference at the narrowest point between costal margin (xipho-sternum) and the iliac crest at the end of gentle expiration and measuring hip circumference at the level of greater trochanter (the maximal circumference) in standing position and at normal expiration. Then, waist/hip ratio was calculated by dividing the waist circumference and / the hip circumference before and after the end of the treatment in both groups (A&B).

4- Blood samples:
Blood samples were obtained between 7:30 a.m. and 8:30 a.m., after overnight fasting (12 hours) during the early follicular phase (days 2–5) of a progesterone-induced menstrual cycle. Plasma LH, FSH, and total testosterone levels were measured using specific radioimmunoassay. Blood insulin and glucose levels were measured with a solid-phase chemiluminescent enzyme immunoassayon.

B) Treatment procedures:
I- Metformin drug: All girls in the two groups (A&B) girls received metformin drug at a dose of 500 mg orally twice daily, 20 min before lunch and dinner for 24 weeks.

II- Aerobic exercise:
All girls in group (B) participated in moderate aerobic exercise program for 24 weeks.

1-Warming up phase:
This phase was conducted through performing walking on electronic treadmill without inclination with 10 minutes warming up 30-40% of Maximum Heart Rate (MHR) as a preparation for the more strenuous activity associated with the second phase of the exercise program to avoid any muscle injuries.

2-The main exercise phase:
This phase was conducted through performing walking on electronic treadmill for 30 minutes. The speed started from 60% and increased gradually to 70% of maximum heart rate (MHR) at the end of 24 weeks.

3- The cool down phase:
This phase was conducted through performing slow movements, similar to those in the warm up phase for 5 minutes at 30-40% of Maximum Heart Rate (MHR), as recovery from the more strenuous activities of the main exercise phase.

Statistical analysis:
Results are expressed as mean ± standard deviation. Test of normality, Kolmogorov-Smirnov test, was used to measure the distribution of data measured pre-treatment. Accordingly, comparison between variables in both groups was performed using either unpaired t test or Mann-Whitney test whenever it was appropriate. Comparison between variables evaluated at the beginning and at the end of cure in the same group was performed using either paired t test or Wilcoxon signed ranks test whenever it was appropriate. Statistical Package for Social Sciences computer program (version 19 windows) was used for data analysis. P value ≤ 0.05 was considered significant.

RESULTS

Physical characteristics of the patients:
There was no significant difference between mean values of age pre- treatment in both groups A and B, with t value 0.198 and p value 0.844.

II- BMI, LH, FSH, LH/FSH ratio, total testosterone, fasting blood glucose (FBG), fasting blood insulin (FBI), fasting blood glucose/fasting blood insulin ratio (FBG/FGI ratio) and menstrual cycle interval within groups:

Table (1): BMI, LH, FSH, LH/FSH ratio, total testosterone, fasting blood glucose (FBG), fasting blood insulin (FBI), fasting blood glucose/fasting blood insulin ratio (FBG/FGI ratio) and menstrual cycle interval between groups pre ttt.

	BMI	Waist/ hip ratio	LH	FSH	LH/FSH ratio	Total testosterone	FBG	FBI	FBG/ FBI ratio	Menstrual cycle Nterval
Group (A)	22.91±1.31	0.81±0.03	12.16±2.23	4.67±0.69	2.59±0.23	0.77 ± 0.07	89.24±3.72	18.06±2.19	5.00 ± 0.56	77.40 ±31.63
Group (B)	23.20±0.96	0.83±0.04	12.30±1.39	4.54±0.41	2.67 ±0.31	0.78 ± 0.06	87.72±3.82	18.44±1.16	4.77 ± 0.36	74.60± 30.14
T value	-0.884	-1.620	-0.255	0.800	-0.931	-0.332	1.424	-0.775	1.721	-0.487
P value	0.381 (NS)	0.112 (NS)	0.800 (NS)	0.428 (NS)	0.356 (NS)	0.741 (NS)	0.161 (NS)	0.444 (NS)	0.093 (NS)	0.627 (NS)

Data are expressed as mean ± SD. Z= Mann Whitney test. S= p< 0.05= significant; NS= p> 0.05= not significant.

Table (2): BMI, LH, FSH, LH/FSH ratio, total testosterone, fasting blood glucose (FBG), fasting blood insulin (FBI), fasting blood glucose/fasting blood insulin ratio (FBG/FGI ratio) and menstrual cycle interval between groups post ttt.

	BMI	Waist/ hip ratio	LH	FSH	LH/ FSH ratio	Total testosterone	FBG	FBI	FBG/ FBI ratio	Menstrual cycle Interval
Group (A)	22.01 ± 1.49	0.78 ± 0.03	10.34±2.24	5.16±0.69	1.99±0.22	0.62 ± 0.08	82.96±3.73	12.24±2.39	7.01 ±1.30	61.96± 24.53
Group (B)	20.94 ± 0.99	0.77 ± 0.03	7.65 ± 1.39	5.92±0.34	1.29±0.21	0.52 ± 0.06	73.40±3.94	10.84±1.07	6.83 ±0.71	45.76± 17.83
T value	2.986	0.777	5.106	-5.029	11.314	5.089	8.820	2.678	0.620	-3.244
P value	0.005 (S)	0.441 (NS)	0.001 (S)	0.001 (S)	0.001 (S)	0.001 (S)	0.001 (S)	0.011 (S)	0.539 (NS)	0.001 (S)

Data are expressed as mean ± SD. Z= Mann Whitney test. S= p< 0.05= significant; NS= p> 0.05= not significant

A-Within groups:

There was a statistical significant decrease in the mean value of BMI,LH, LH/FSH ratio, total testosterone, FBG, FBI, FBG/FGI ratio and menstrual cycle interval post treatment in group A and group B. There was a statistical significant increase in the mean value of FSH post treatment in group A and group B.

B-Between groups:

Pre-treatment, there was no statistical significant difference between the mean value of BMI, LH, FSH, LH/FSH ratio, total testosterone, fasting blood glucose (FBG), fasting blood insulin (FBI), fasting blood glucose/fasting blood insulin ratio (FBG/FGI ratio) and menstrual cycle interval between both groups A and B (Table 1).

Post treatment, there was significant difference in FSH (more increase in group B). There was significant difference in weight, BMI, LH, LH /FSH ratio, Total Testosterone, fasting blood glucose, fasting blood insulin and menstrual cycle B-interval (more decrease in group B). There was no significant difference in waist / hip ratio and fasting glucose /insulin ratio (Table 2).

DISCUSSION

Polycystic ovary syndrome (PCOS) is a prevalent disorder that affects approximately 10% of women of childbearing age (Asunción et al. 2000) with classic features of anovulatory infertility, menstrual dysfunction, and hirsutism (Azziz et al., 2004)**.** Other important manifestations include metabolic abnormalities, including insulin resistance and dyslipidemia, low-grade inflammation, an increased risk of type 2 diabetes, and cardio metabolic risk particularly in the presence of obesity [(Balen, 2001) and (Fearnley et al., 2010) and (Toprak et al., 2001)].

Despite the potential beneficial effects of exercise in PCOS, it is not fully investigated in non-obese women. So, this study was conducted to determine the effect of aerobic exercise on non-obese adolescent girls with polycystic ovarian syndrome (PCOS).

Results showed that there was a statistically significant decrease in the mean value of weight, BMI, waist circumference, hip circumference, waist / hip ratio, LH, LH /FSH ratio, Total Testosterone, fasting blood glucose, fasting blood insulin, fasting glucose /insulin ratio and menstrual cycle interval in both groups A&B post-treatment. There is a statistically significant increase in FSH in both groups A&B post-treatment. When comparing both groups together post-treatment, there is a significant difference in FSH (more increase in group B), weight, BMI, waist circumference, hip circumference, LH, LH /FSH ratio, Total Testosterone, fasting blood glucose, fasting blood insulin and menstrual cycle interval (more decrease in group B), there is no significant difference in waist / hip ratio and fasting glucose /insulin ratio.

The results of this study agreed with (Turan et al., 2015)**,** who investigated the effects of 8 weeks of structured exercise program on non-overweight patients with PCOS. They found that 8 weeks of structured exercise was effective for improving anthropometric, cardiovascular, and metabolic parameters and for regulating menstrual cycles in non-overweight patients with PCOS, despite the absence of significant changes in sex hormones.

The absence of significant changes in sex hormones in (Turan et al., 2015) may be due to short term exercise intervention (8 weeks) in their study, but we used long term exercise intervention (24 weeks).

Slim women improve insulin resistance after eight weeks of exercise may be that there is a simultaneous reduction in waist-hip ratio, assuming the goal to one some degree reflects the amount of visceral fat (Turan et al., 2015).

The improvement in body composition, with little or no effective change in total body weight, may be related to the concomitance of the increase in lean muscle mass and reduced body fat promoted by this type of exercise (Hunter et al., 2002).

The result of this study supported by Bisgaard and Dela, (2017) who performed randomized controlled trial and showed that structured physical exercise, can improve insulin sensitivity, hyperandrogenemia and menstrual frequency in lean women with PCOS.

The results of this study also supported by Hoeger et al., (2008), who studied the effects of 12-week exercise training program, aerobic exercise at 60- 80% of maximal heart rate, 25-30 min/day, 3 days/week on 40 PCOS patients 20 were lean (BMI<20) and 20 were obese (BMI>25). Menstrual condition (menses cycle) in obese and thin women has improved after sport activity (p value<0.0001, p value =0.028).

The number of follicles existing in right and left ovaries had significant decrease in experimental group of both obese and thin women.

Aerobic exercise (12-24 weeks) at moderate intensity results in significantly increased insulin sensitivity, improved parameters for hyperandrogenism and increased menstrual frequency, even with a minimal weight loss (Hoeger et al., 2008).

(Kogure et al., 2016) found that resistance exercise alone can improve hyperandrogenism, reproductive function, and body composition by decreasing visceral fat and increasing lean muscle mass.

The results of the current study are in agreement with those of (Vigorito et al., 2007), who reported that after 3-month exercise training program, young PCOS women showed a significant reduction in BMI and improvement in insulin sensitivity indexes.

The study results are also supported by (Palomba et al., 2007) who showed that a 24-week aerobic exercise program or a hypo caloric high-protein diet improved both menstrual cycle and fertility in PCOS patients, and increased ovulation rates and menses frequency as well as, induced greater improvement in waist circumference and sex hormones.

Also, The results of the present study were goes in harmony with those of Bruce et al., (2004), who suggested that moderate aerobic exercise as a treatment for clinical complications in PCOS may be favorable, considering the beneficial effects of exercise in other insulin resistant- population, independent of weight loss. Also, (Harrison et al., 2011) demonstrated the positive effects of exercise training programs on maximal oxygen consumption, weight, and waist circumferences in PCOS patient.

The results of this study agreed with results achieved by (Luciano et al., 2002), who reported that fasting insulin was assessed as a measure of IR, with most studies reporting improvements following intervention, consistent with enhanced insulin sensitivity within skeletal muscle following exercise.

The study results are agreed with (Liza et al., 2014), who reported that exercise alone and lifestyle intervention is beneficial for improving FSH profile and reducing total testosterone. The study results are also agreed with (Jedel et al., 2011) and (Vigorito et al., 2007), who found that total testosterone levels were reduced in both the exercise-alone and lifestyle intervention.

Also**,** (Fux et al., 2010) found that a small decrease in body weight trough lifestyle changes was enough to improve menstrual cycles in these PCOS women and that metformin offered additive effects regarding insulin resistance and hyperandrogenism.

The results of this study are agreed with Gambineri et al., (2002), who reported that weight loss in PCOS women may decrease LH pulse amplitude which, in turn, can followed by reduced androgen production. Also, the key factor responsible for these effects is the reduction of the insulin level which obviously associated with an improvement of insulin resistant state (Moran et al., 2003).

The role of non-pharmacological therapy in PCOS patients has been evaluated in several studies. (Giallauria et al., 2008) assigned 124 PCOS patients to 2 groups for a 3-month exercise program. They demonstrated that exercise improved autonomic function and inflammatory patterns. In a similar study (based on 90 young women with PCOS who were randomly divided into 2 groups (Vigorito et al., 2007), reported that patients who participated in a 3-month structured exercise program exhibited improvements in cardiopulmonary functional capacity. Other studies have reported greater reductions in BMI (Liao et al., 2008), but we did not focus on weight loss, as the patients were not overweight. Nevertheless, they experienced important changes in several cardiovascular parameters and in BMI, Waist/Hip ratio, LH, FSH, LH/FSH ratio, Total Testosterone and Insulin sensitivity.

Alternatively, exercise interventions in PCOS show mixed results in their effects on hormonal profiles. The results of this study disagreed with (Vigorito et al., 2007) and **(**Bruner et al., 2006), who found no changes after 12–24 weeks of combined nutritional counseling and aerobic or resistance exercise.

CONCLUSION

On the basis of the data obtained in the present study, we concluded that aerobic exercise is very effective in non-obese adolescent girls with polycystic ovarian syndrome. Long-term regular exercise provides betters results in reproductive and metabolic parameters and improve menstrual irregularity in non-obese adolescent girls with PCOS and consequently improve the quality of life of these patients.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

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AUTHOR CONTRIBUTIONS

DsM and MAA performed data collection and wrote the manuscript. MAA, HMH and HHK put the design. DsM and MAA performed experiments HMH and HHK reviewed the manuscript and reviewed statistical analysis. All authors read and approved the final version.

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