

Original Article

The Effect of Home based Exercise on Treatment of Women with Poly Cystic Ovary Syndrome; a single-Blind Randomized Controlled Trial

Farzaneh Vasheghani-Farahani¹, Shahrzad Khosravi*¹, Amir Hossein Abedi Yekta¹, Mohsen Rostami¹, Mohammad Ali Mansournia¹

¹ Sports Medicine Research Center, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran

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Abstract

Background: The most common reproductive endocrine disorder of reproductive age women is a Poly cystic ovary syndrome (PCOS) Metabolic syndrome has been more reported in patients with PCOS in comparison to general population. Few investigations have been performed to evaluate the independent effect of exercise on biochemical and clinical symptoms of patients with PCOS. The aim of the study was to find the effect of home base aerobic-strengthening exercises on anthropometric and hormonal variables of patients with PCOS.

Materials and Methods: In this randomized controlled trial twenty women in the exercise group performed aerobic, strengthening exercises; the other 20 participants in the control group were advised to continue their previous physical activity pattern. Blood pressure, Waist to Hip ratio (WHR), BMI along with hormonal variables (including insulin related factors, sexual hormones and inflammatory factors) were assessed at baseline and after the 12 week intervention).

Results: 16 patients in the exercise group and 14 patients in control group finished the study. The WHR ($p < 0.001$) along with the blood level of insulin ($p = 0.016$), FBS ($p = 0.044$), Prolactin ($p = 0.022$) and hsCRP ($p = 0.035$) and HOMA index ($p = 0.009$) were decreased significantly in the exercise group compared with the control group. No significant differences were found in lipid profile and sexual hormones between groups at the end of the study.

Conclusion: We can conclude that 12 weeks combined aerobic-strengthening exercise program in women with poly cystic ovary syndrome can lead to a reduction of waist to hip ratio (WHR) and some cardiovascular risk factors (including insulin, FBS, HOMA index and HsCRP) along with an increase of prolactin level in these patients.

Keywords: Poly cystic ovary syndrome, Physical activity, Insulin resistance, Women, Pregnancy

*Corresponding Author: Shahrzad Khosravi, MD, Sports Medicine Specialist, Shahid Beheshti University of Medical Science, Tehran, Iran. E-mail: shahrzadekhosravi@yahoo.com.

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Introduction

The most common reproductive endocrine disorder of reproductive age women is Poly cystic ovary

syndrome (PCOS). It has been reported that about 10 percent of premenopausal women are affected by this disorder¹. In addition to the irregularity of menstrual

periods, infertility (due to anovulation) and hyperandrogenic state which might lead to presentation of hirsutism in the patients², women with PCOS are at higher risk of some chronic systemic diseases³. Metabolic syndrome and its related components, including hyper lipidemia, obesity and increased waist circumference have been more reported in patients with PCOS in comparison to general population⁴. The patients with PCOS are also at higher risk of Cardiovascular diseases and type 2 diabetes³. Although there is a discrepancy regarding the prevalence of obesity among women with PCOS (from 33% to more than 50%)^{4,5}, the studies have shown a higher prevalence of obesity among women with PCOS in comparison to general population⁵.

The burden attributable to PCOS and its related complications is great. Therefore, considerable research efforts have been made to find effective treatments for this disease and to reduce its economic load. Available pharmacological treatments in PCOS mostly address the insulin resistance and ovulatory dysfunctions of the patients. However, life modification interventions are still the first choice in the treatment of these patients⁶. Although the pathogenesis of PCOS is still under discussion, Hyper insulinemia due to insulin resistance state is suggested as the major factor in the development of most of symptoms and implications of PCOS⁷. Obesity contributes in development of insulin resistance state among the patients⁸. In light of this finding, the dietitians have tried to control the complications of PCOS through weight loss of the patients^{4,5}. Modifying the lifestyle of the patients in the aim of induction of weight loss in the patients with PCOS have also been highlighted by some studies⁹. According to published reports, the effectiveness of lifestyle modification is comparable with medical therapy¹⁰. Other studies have evaluated the effect of dieting alone or simultaneous diet and physical activity on weight loss and thereby biochemical factors and symptoms of the patients with PCOS¹¹. These studies have found this therapeutic regimen effective in treatment of patients with PCOS^{12,13}. In this regards, it has been reported that 5 percent weight loss in overweight women might lead to a reduction of insulin and testosterone

serum level of the patients with PCOS. Physical activity has been recommended as long term weight maintainer when is combined with diet for weight loss of the patients¹⁴ and its role in weight loss (when prescribed alone) is still in doubt.

To the best of our knowledge only few investigations have been performed to evaluate the independent effect of exercise on biochemical and clinical symptoms of patients with PCOS. Therefore the aim of the current randomized controlled trial was to investigate the effect of home-based aerobic-strengthening exercise as an independent therapeutic program of biochemical and clinical presentations of women with PCOS.

Methods

This study was designated as a controlled randomized trial in Sports Medicine Research Center of Tehran University of Medical Sciences. Ethical approval of this study was obtained from the Ethical Committee of Tehran University of Medical Sciences. The study was registered as number "IRCT138902073819N1" a registry of clinical trials (i.e. Irct.ir). All the participants signed the written informed consent.

We calculated the sample size of the study using the following formula: $n=2*(Z1-\alpha/2*Z1-\beta)^2*\sigma^2/d^2$. With $\alpha=0.05$; $1 - \beta$ (or power of the study) =0.80; σ (the variance of severity of insulin resistance in the study group) =3; and d (the difference in insulin resistance between the 2 groups) =2, at least 13 participants were needed in each group. Since we were expecting that 30% of recruited patients could not be eligible for the final analysis of the study, 20 patients were enrolled in each group (totally 40 subjects). In this regards, eligibility of 63 patients was assessed to find 40 participants of the study.

Participants who met the inclusion criteria of the study (Box 1) were referred to our clinic from gynecologic clinic of Imam Khomeini hospital, an educational hospital affiliated with Tehran University of Medical Sciences. The 40 recruited participants were blocked randomized in blocks of 6, into 2 following groups: Control Group and exercise group.

Patients in the exercise group were asked to walk with a medium intensity (64 to 76% of maximum heart rate) for 30 minutes per day and at least 5 days per week. In this regards, the subjects were previously

Box 1. Inclusion and exclusion criteria of the study**Inclusion criteria**

- Existence of at least two of three following clinical or biochemical conditions
 - a. oligo or anovulation
 - b. clinical and/or biochemical signs of hyperandrogenism
 - c. poly cystic ovaries
- Ruling out related disorders including congenital adrenal hyperplasia, Cushing Syndrome and Androgen Secreting Tumors
- Age 15-40 years
- Duration of Symptoms > 6months

Exclusion criteria

- Contraindications of exercise
- Endocrine disorders including Hyperprolactinemia and hyperthyroidism
- Depression
- Inability in attending the follow-up sessions of the study
- Any systematic, hepatic, renal or cardiovascular diseases such as: diabetes, restrictive lung diseases, heart diseases and renal failure
- Use of any of following medicines in past 30 days: Oral contraceptive pills (OCPs), Anti diabetic pills, Ovulation inducing/anti androgenic medications or any substance containing corticosteroids
- Pregnancy
- Smoking or alcohol drinking

taught how to measure their radial pulse rate manually. The maximum heart rate was defined as $(0.85) \times (220 - \text{age})$ for each person. In addition, the participants in the exercise group were required to perform strengthening exercises 3 days per week; biceps Curl, wall push up, Chair push up and Single Arm Row were the planned exercises for the upper limb. For strengthening the lower limb of the participants Seated lower leg lift, Seated Straight leg

lift, Stair Step and Chair Squat exercises were considered. The participants were asked to practice each of the mentioned strengthening exercises 10 times per each bout.

The number of bouts per day was increasing gradually in the course of the study; the participants started the study with one bout per day while at the last week of the study, they were practicing strengthening exercises, 3 bouts per day. The patients in the exercise

group were asked to perform the first two bouts of exercises under supervision of the investigators to set the standards of exercise according to supposed protocol for the participants. During the course of the study, each 2 weeks the researchers made a call to the participants of exercise group and encouraged them to continue the study protocol. The participants in the control group were instructed to resume their normal activities.

Before and after finishing the study, blood samples were collected from all the participants to compare the level of follow biochemical or hormonal factors between the groups; Cholesterol (CHL), Prolactin (Pro), Thyroid Stimulating Hormone (TSH), Testosterone, 17-Hydroxy Progesterone (17-OHP), High sensitivity C Reactive Protein (hcCRP), Triglyceride (TG), Insulin (Ins) and Fasting Blood Glucose (FBS). In this regards, an expert nurse took the blood samples and sent the samples to a reliable biochemical and hormonal laboratory of Imam Hospital. At the beginning and 12 weeks after the study, Weight, Body Mass Index (BMI), Waist Circumference, and waist to hip ratio (WHR) of all participants were measured according to standard protocols. The nurse who took the blood samples and the assessor who measured the waist and hip circumferences and weight of the subjects were not aware of the allocation status of the study.

Each two weeks, according to the self-records of the participants in their logbooks, their adherence to the designed therapeutic protocol during the last 24 hours were collected. These data were used to analyze the level of adherence of patients in the physical activity group to their prescribed exercise program. In case of the remarkable difference between patients' physical activity with the previously recommended exercise program, proper suggestions were provided.

Data analysis was performed using SPSS 16 (SPSS Inc, Illinois, US). ANCOVA (analysis of covariance) model was used for quantitative analysis of the data. Chi-square and fisher exact test were used for analysis of qualitative data. The results were considered as significant if the p value was 0.05 or less.

Results

During the course of the study, 63 subjects referred to our center. Forty patients were randomly assigned equally (n=20) to control and exercise groups (Figure 1). As it is shown in figure 1, 16 patients in exercise group and 14 patients in the control group completed the study and their data were included in final analysis. The patients in control and exercise groups had a mean age SD of 29 ± 5.39 years (range: 22 to 38) and 27.7 ± 4.2 years (range: 21 to 36) respectively. Of the patients in exercise group 12 and of those in the control group 10 patients had referred to the gynecology clinic with the chief compliance of infertility. In the exercise group, at the end of the study, 4 women got pregnant (4 of 12 women). However, no patient got pregnant in the control group. The difference was not statistically significant ($p=0.096$).

It was found that the waist to hip ratio decreased significantly in the exercise group ($p<0.001$) compared with the control group. However the between group difference of reduction of BMI of the subjects was not statistically significant ($p=0.074$) although the BMI of patients in the exercise group decreased more than other groups.

Regarding biochemical and hormonal factors, it was found that the blood level of hsCRP and FBS decreased significantly in the exercise group ($p=0.035$ and $p=0.044$ respectively) compared with the control group. In addition, Comparing the groups, significantly more reductions were found in both the insulin level and HOMA index ($FBS * Insulin / 405$) of exercise group ($p=0.016$ and $p=0.009$ respectively) (Table 2). Our data also showed a significant increase in the Prolactin level in the exercise group after 12 weeks of the study ($p=0.022$).

According to self-records of physical activity of the patients in their log book it was found that the patients in the exercise group had a mean adherence of 76% and 64% to aerobic and strengthening exercises respectively.

Discussion

We found that the level of insulin, FBS and HOMA index decreased significantly among patients with PCOS after 12 weeks home based exercise, including both strengthening and aerobic components. In

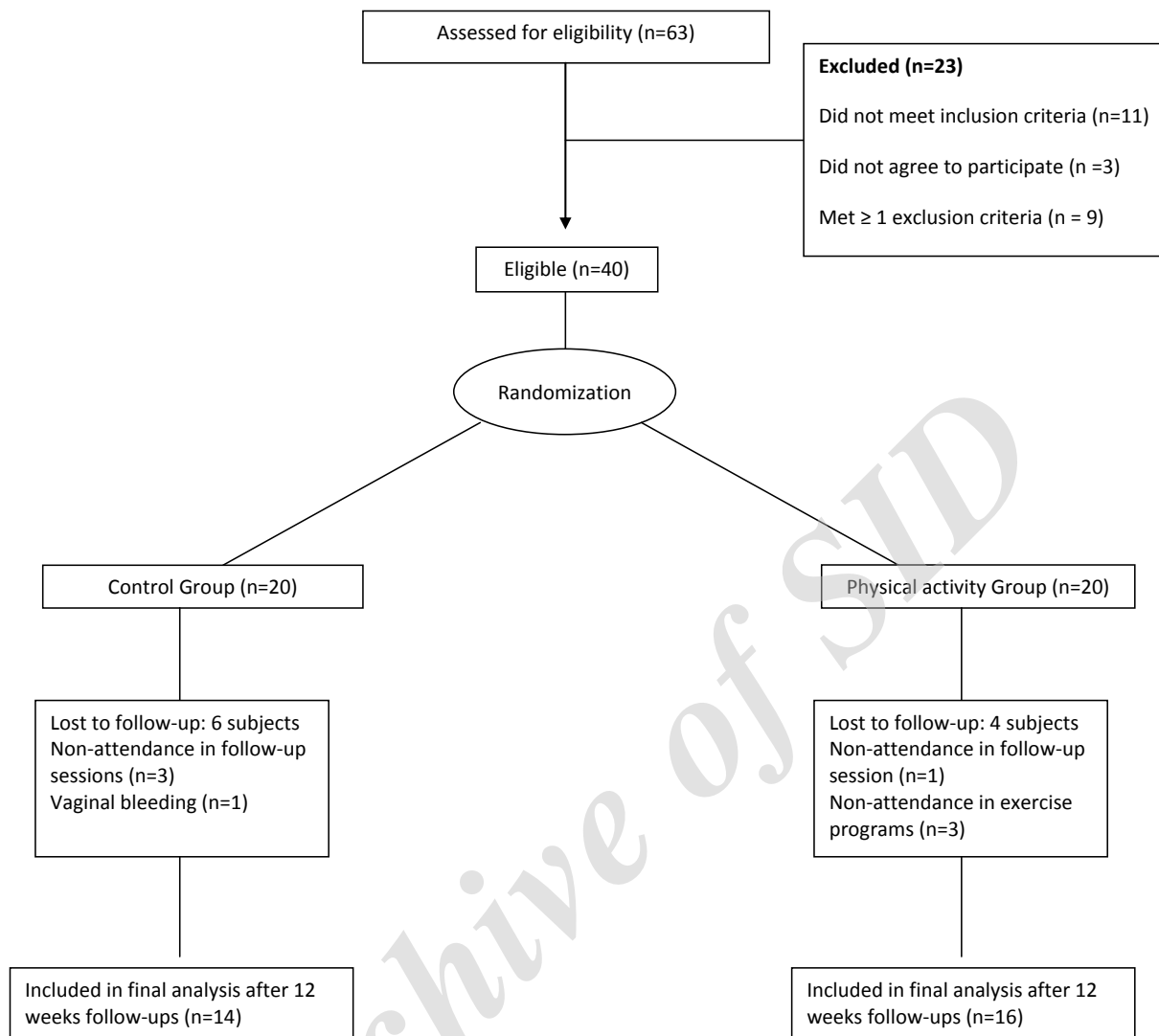


Figure 1. Flow chart of patients in two groups.

addition, in exercise group, significantly the blood level of hsCRP was decreased more and blood prolactine level was increased more in comparison to controls. However, no more significant reduction was found in lipid profile, 17(OH) progesterone, TSH and testosterone level of home based exercise group compare to the control group.

The effect of combination of aerobic and resistance exercise in improvement of insulin sensitivity in patients with type 2 diabetes has been shown by other investigators^{15,16}. Hollmann M et al.¹⁷ as in study by Moran LJ and his colleagues¹⁸ showed the positive effect of weight loss on improvement of fertility function and insulin resistance in patients with PCOS. The effectiveness of physical activity in

weight loss of patients with PCOS has also been shown in different studies¹⁸⁻²⁰. Although the role of energy restriction in weight loss has been reported before, physical activity as one of the components of weight management programs is mostly recommended to prevent weight regain of the patients²¹. The results of our study, showed the independent effect of physical activity in the decrease of insulin resistance of patients with PCOS. In addition, HOMA index and FBS of patients in the exercise group were decreased more than other group (P=0.009 and 0.044 respectively). These results are in consistency with most of previously performed studies^{11,20}, although the exercise programs performed by participants in these studies were different. According to the study

Table 1: Change in BMI and WHR in two groups.

Outcome measures	Control group	Physical activity group	Difference in mean (95% CI)	P value
BMI (kg/m²)				
At baseline	25.7±2.15	28.8±5.88		
12th week	25±2.06	28.07±5.7	0.182 (-0.91to1.27)	0.0735
WHR				
At baseline	0.845±0.11	0.804±0.077		
12th week	0.840±0.11	0.756±0.074	-0.044 (-0.031to-0.058)	<0.001

BMI: Body Mass Index, WHR: Waist to Hip Ratio

performed by Vigorito C et al.²⁰, after 3 months of intervention, both of structured and hospital based exercise programs (3 sessions per week for 3 months) lead to decrease of 17 α -hydroxyprogesterone and testosterone of patients with PCOS, although the differences between two groups were not significant (p=0.25 and p=0.14 respectively). These data are in consistency with those were found in our study. Regarding the lipid profile of the patients with PCOS which is associated well to the insulin resistance of these patients, Brown LJ et al.²² showed a significant reduction in the blood level of VLDL, Triglyceride and HDL of patients who received a therapeutic and a well controlled exercise program. In the study by Vigorito C et al.²⁰ (structured and hospital based exercise program) as in our study (home based exercise program), no significant relation was found in components of the lipid profiles of the patients. Brown LJ et al.²² set the heart rate of the patients in a way to achieve 50% maximal VO₂ in all exercise sessions, while in our study and the study by Vigorito C et al.²⁰ the intensity of the exercises were different (64-76% of maximal heart rate and 60_70% of VO₂ max respectively).

In this study, waist to hip ratio (WHR) of patients in the exercise group decreased significantly more than the control group after 3 months. The role of physical activity in the reduction of WHR of patients with PCOS has been shown in other studies^{20,23}. In a prospective cohort study, using unsupervised exercise program.

Randeva HS et al.²³ showed the favorable effect of their program in a decrease of WHR of patients with PCOS. However, their exercise program was containing only brisk walking with light to moderate

intensity. In our study, we used both aerobic and strengthening exercises. In addition, the frequency and intensity of exercise program used in our study were more than that used by Randeva HS et al.²³. While WHR is shown to decrease in most of conducted studies which have used structured and supervised exercise programs^{11,19,20}, to best of our knowledge, this is the first randomized controlled study, shows the effectiveness of home-base exercise program in a decrease of WHR of patients with PCOS. The combined exercise protocol used in the current prospective study was similar to the aerobic and resistance exercise program used in the study by Thomson RL et al.²⁴. They showed the effectiveness of this protocol along with aerobic exercises alone in decrease of fat mass and BMI of the patients with PCOS.

The rate of drop out of this study was 25%, which can be considered as one of the limitations of the study, although this rate was lower than that reported in the STRRIDE study²⁵. The small sample size of the study along with the short course of follow-up of the study can be considered as another limitation in this study. Menstrual behavior of the participants was not included in outcomes of the study, while in other studies, this index has also been evaluated. As it is mentioned before, of the subjects in exercise group, 4

of them got pregnant after finishing the study. However, pregnancy was not reported in any of subjects in control group. Although this difference was not significant (p=0.96), this might imply of improvement of menstrual behavior of patients in the physical activity group in comparison to control group.

Table 2: Difference in biochemical and hormonal factor between two groups.

Outcome measures	Control group	Physical activity group	Difference in mean (95% CI)	P value
Prolactin (ng/ml)				
At baseline	9.15±2.49	11.53±6.49		
12th week	13.69±8.17	35.10±31.4	21.99 (3.39to40.58)	0.022
TSH (mIU/L)				
At baseline	2.37±1.75	2.48±1.30		
12th week	4.01 ±5.1	2.41±0.096	-0.237 (-0.732to0.259)	0.336
17(OH) Progesterone (ng/ml)				
At baseline	1.57±0.64	2.37±2.39		
12th week	1.99±0.87	3.14±2.35	1.110 (-0.318to2.53)	0.122
Testosterone (ng/ml)				
At baseline	0.655±0.202	0.717±0.22		
12th week	0.66±0.21	0.87±0.79	0.102 (0.183to0.386)	0.471
hsCRP (mg/l)				
At baseline	2.96±2.95	3.55±3.63		
12th week	2.8±2.2	1.99±2.52	-1.196 (-2.252to0.086)	0.035
TG(mg/dl)				
At baseline	186.14±87.63	194.37±98.79		
12th week	167.42±77.10	222.12±133.3	48.003 (-13.581to109.58)	0.121
Cholestrol (mg/dl)				
At baseline	176.57±30.11	186.5±49.40		
12th week	175.28±32.38	178.87±49.30	-2.833 (-22.88to17.218)	0.774
LDL (mg/dl)				
At baseline	107.71±20.67	112.5±29.58		
12th week	109.78±23.36	102.43±26.09	-10.665 (-23.83to2.501)	0.108
HDL (mg/dl)				
At baseline	52.64±6.02	57.93±12.30		
12th week	49.57±7.9	59.12±13.84	7.148 (-1.233to15.328)	0.091
FBS(mg/dl)				
At baseline	110.35±23.61	99.6±15.7		
12th week	104.71±23.36	87.81±9.33	-10.963 (-0.3092to-21.61)	0.044
Insulin (mU/L)				
At baseline	15.10±9.94	9.6±6.1		
12th week	16.94±9.1	8.48±4.32	-5.939 (-1.204to-10.674)	0.016
HOMA Index				
At baseline	4.5±4	2.41±1.76		
12th week	4.5±2.8	1.82±0.92	-2.003 (-0.542to-3.464)	0.009

Conclusion

We can conclude that 12 weeks combined home based aerobic-strengthening exercise program in women with poly cystic ovary syndrome lead to decrease of waist to hip ratio (WHR), some cardiovascular risk factors (including insulin, FBS and HOMA index and hsCRP) and increase of prolactine level of patients with PCOS. It can be suggested that further randomized controlled studies should be conducted to compare the effect of different combined or single exercise protocols with life modifying and also pharmacological interventions on treatment of patients with PCOS.

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