ORIGINAL ARTICLE

Effects of supervised aerobic training on the levels of anti-Mullerian hormone and adiposity measures in women with normo-ovulatory and polycystic ovary syndrome

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Abstract

Objective: To evaluate the change in the levels of anti-Mullerian hormone, adiponectin, weight loss and fertility parameters in obese women with or without polycystic ovary syndrome, following 12 weeks of supervised aerobic exercise.

Methods: This study was conducted from August 2013 to October 2014 among obese women with or without polycystic ovary syndrome referred to Obstetrics and Gynecology clinic, Mansoura University Hospital, Faculty of Medicine, Mansoura, Egypt. Patients were classified into three age-matched groups; group A had controls, group B had patients with polycystic ovary syndrome and group C had obese women. Anti-Mullerian hormone, adiponectin, follicle-stimulating hormone, oestrogen, fasting insulin, fasting glucose, homeostasis model of assessment of insulin resistance, antral follicle count, hirsutism score, weight, menstrual cyclicity and ovulatory function were assessed at baseline and following 12 weeks of supervised aerobic exercise. Statistical analysis was performed using SPSS 17.

Results: Of the 90 patients, there were 30(33.3%) in each group. The mean age was 28.7±3.84 years in group A, 27.9±4.1 years in group B and 27.6±5.7 in group C. The 30(33.3%) participants who responded to aerobic exercise interventions showed significant improvements in reproductive function), with lower baseline anti-Mullerian hormone levels, greater weight loss and higher adiponectin level compared to the the 30(33.3%) participants who did not respond to the exercise programme. Weight loss, fertility hormones, follicle-stimulating hormone, prolactin, oestrogen, antral follicle count, baseline anti-Mullerian hormone, and adiponectin were significantly correlated to the improvement in reproductive function ($p<0.05$ each). The change in anti-Mullerian hormone and adiponectin levels correlated significantly with physical activity level in both responders and non-responders ($p<0.05$). In women with anovulatory syndromes, there were significant improvements in ovarian process with an ovulation rate of 13(43.3%) and a restoration of menstrual cycle with a rate of 17(56.7 %) following 12 weeks of supervised aerobic exercise.

Conclusion: Moderate aerobic training for 12 weeks had a positive significant effect on reproductive functions via modulating adiposity, the levels of adiponectin, anti-Mullerian hormone and fertility hormones.

Keywords: Polycystic ovary syndrome, PCOS, Aerobic exercise, Anti-Mullerian hormone, AMH, Obesity. (JPMA 67: 499; 2017)

Introduction

Many studies reported good reproductive functions among women with optimal body weight (BW) compared to those with obesity who are more likely to experience reproductive problems, including menstrual disorders, infertility, anovulation and maternal complications during pregnancy.[1-6]

Polycystic ovary syndrome (PCOS) is the most common cause of anovulatory infertility in women of reproductive age, affecting about 7% of this population. The aetiology of PCOS is closely linked to obesity and abdominal adiposity that are considered to worsen the clinical presentation, particularly menstrual irregularities and hyperandrogenism.[6,7] Recently, it was reported that new roles of adipokines such as leptin, adiponectin and resistin emerged in the field of fertility and reproduction by regulating the functions of gonads and the hypothalamic-pituitary axis.[8,9]

In PCOS patients, the levels of adipokines are still controversial; a few reports have summarised the effects of adiponectin on the reproductive organs, either at a molecular level or for clinical relevance.[10,11] lower level of adiponectin was reported in obese women with or without PCOS compared with healthy control subjects of a similar body mass index (BMI).[12,13] Similarly, serum anti-Müllerian hormone (AMH) levels were reported to measure ovulation rates in overweight and obese women with PCOS women, whereas it released from the granulosa cells into both pre-antral and antral follicles.[14] It

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was reported that women with significantly lower baseline AMH levels experienced menstrual improvements compared with those who have menstrual disorders with higher AMH levels. The decline in serum AMH levels was correlated with age, the number of antral follicles and the ovarian response to hyper stimulation.[15,16]

Weight loss via exercise or diet is considered one of the most important targets in lifestyle modification programmes capable to induce an improvement in reproductive function among obese women with PCOS.[17] Exercise interventions of moderate activity are one of the most important lifestyle modifications that positively influence on fertility and assisted reproductive technology (ART) outcomes.[18] It was shown that implantation rates, pregnancy and a reduction in the risks of miscarriage were reported among women undergoing intra-cytoplasmic sperm injection (ICSI) following exercise training for at least one hour three times per week.[19] Also, low to moderate exercise was also associated with increased implantation and live birth rates in women undergoing ART.[20] Studies of the effects of 12- to 24-week lifestyle interventions comprising diet, exercise and/or behavioural changes in overweight infertile women with or without PCOS,[2,21] showed a significant improvement in ovulatory, menstrual regularity and reduced risk of miscarriage compared to pre-intervention.[22]

Little is known about the effects of supervised aerobic training (SAT) on the level of AMH and adiponectin which may have a role in improvements of reproductive function in obese women with or without PCOS. The current study was planned to evaluate the effect of supervised aerobic exercise (SAE) interventions for 12 weeks on adiposity measures, AMH and adiponectin levels, and to study the possible correlation with adiposity, clinical and hormonal parameters in PCOS and normo-ovulatory women.

Subjects and Methods

This study was conducted from August 2013 to October 2014 among obese women with or without polycystic ovary syndrome aged between 20 and 35 years referred to Obstetrics and Gynecology clinic, Mansoura University Hospital, Faculty of Medicine, Mansoura, Egypt. Diagnosis of PCOS was established according to Ferriman-Gallwey scores.[23] Based on the presence of elevated serum fertility hormones, disorder in biochemical hyper-androgenism, presence of chronic anovulation and Ferriman score of $\geq$8. Women with an ovulatory infertility were diagnosed according to irregular periods, normal fertility hormones and regular sexual intercourse.[24]

Based on obesity and PCOS diagnosis, participants were classified into three groups: group A were controls with BMI of 20-29 kg/m^2, group B had PCOS and BMI of 30-35 kg/m^2), and group C had obese women with BMI of 30-35 kg/m^2). The control group consisted of healthy women with male, tubal or unexplained infertility. They had regular ovulatory cycles (25-35 days), no endocrine abnormalities, and had normal ultrasonic ovarian morphology. Patients with presence of ovaries, no previous ovarian operation, adequate visualisation of ovaries on transvaginal sonography and no current hormone therapy were included.

Participants with normal BMI, other concomitant diseases such as diabetes, viral infections, current and previous drug administration that affected hormonal levels were excluded.

This study was approved by the ethics committee of the Rehabilitation Research Chair (RRC), King Saud University, Saudi Arabia. Informed consent was obtained from all participants.

Participants were subjected to training interventions programme of treadmill walking, 45 minutes three times per week for 12 weeks. Each individual's training intensity was calculated as the training heart rate (THR) based on the subject's age and predicted maximum heart rate and resting heart rate according to Karvonen's formula, [THR = resting heart rate (HRrest) + (maximum heart rate (HRmax) - HRrest) $\times$ training fraction (TF)], where TF was 65% to 75% for the moderate intensity used in this study. Each exercise session consisted of three phases, i.e. warm-up, active and cool-down phases. The cool-down phase continued for 10 to 15 minutes during which the workload gradually decreased until HR and blood pressure (BP) nearly returned to their resting levels. Throughout the training session, the subjects were monitored by a portable heart rate monitor to keep the exercise intensity within the pre-calculated training heart rate for each subject.[25,26]

Total energy expenditure scores of each patient were calculated from total daily activities collected using pre-validated questionnaire.[27] For each participant, energy scores were calculated based on duration, intensity and frequency of physical activity (PA) performed in a typical week.

According to the response of reproductive functions to exercise interventions, the participants were classified into two groups: responders and non-responders. Responders were characterised by improvements in ovulatory function, menstrual status such as change from irregular cycles to regular cycles or an improvement in

consecutive intercycle variation comparing with non-responders and baseline data.

Comprehensive physical examinations, Ferriman-Gallwey scores,[27] and anthropometric measurements such as BMI, waist circumference (WC) and waist-to-hip ratio (WHR) were estimated in all participants. Serial transvaginal ultrasonographic scans were performed to monitor ovulation at baseline, every 4 days, and successively daily until ovulation in case of a dominant follicle with a mean diameter of ≥12mm. Retrospectively, ovulation was identified by a decrease in follicular dimensions and liquid in the cul-de-sac, and was confirmed by plasma phosphorus (P) and serum oestradiol concentrations assessed before the expected menses on the basis of ultrasonographic results.

Overnight fasting blood samples were taken in the early follicular phase (day 2-3 after the last menstrual period) from all patients and controls for hormone measurement. Serum samples were extracted and stored at -20°C. Assays of serum follicle-stimulating hormone (FSH), oestrogen (E2), prolactin (PRL), adiponectin and AMH, and a transvaginal ultrasound examination for assessment of antral follicle count (AFC) were performed at baseline, 3 weeks and 12 weeks of following moderate aerobic training programme.

Serum FSH and E2 were performed by using mini VIDAS technique and corresponding kits (bio-Mérieux® France). The results were measured and calculated according to the instructions of kits. Serum levels of AMH, PRL, and total adiponectin were determined by enzyme-linked immunosorbent assays (ELISA), (using Beckman coulter Inc., United States; EIA kit, No; 500730, Cayman chemical co., United States; and ADIPOA; ALPCO Diagnostics, Salem, United States kits, respectively).

Homeostasis model of assessment of insulin resistance (HOMA-IR), fasting glucose-to-insulin ratio (GIR) (mg/1024 U), and free androgen index (FAI) were calculated according to standard laboratory assays in all participants before and after each exercise training periods.

A personal daily diary comments such as any adverse effects, together with their severity, duration and any possible cause-effect relationship with the interventions, and the quantity of menstrual bleeding, which was evaluated subjectively by using a rank analogue scale that ranged from 0 (absence of menses) to 5 (normal uterine bleeding) and 10 (severe uterine bleeding) were collected for each participants.

AFC for all participants were counted and calculated during the early follicular phase (cycle day 2 or 3) by using transvaginal ultrasound scanner assay (Philips 11*E; with a 5 MHz probe). In each ovary, the total number of small follicles (2-8 mm) was counted, whereas the sum of the follicle counts in each ovary gave the total follicle count.

Statistical analysis was performed using SPSS 17. The data was evaluated and tabulated as mean and standard deviation (SD). Repeated measure analysis of variance (ANOVA) and Pearson's correlation coefficient were used to evaluate and compare significance of the relationships between the studied parameters. P<0.05 was considered significant.

Results

Of the 90 patients there were 30(33.3%) in each group.

Table-1: Clinical data at baseline and at 3- and 12-week supervised aerobic training follow-ups of obese women with or without polycystic ovary syndrome (PCOS).

Parameters	Group A (Control)	Group B (PCOS)	Group C (Obese)
N	30	30	30
Age (years)			
Baseline	28.7 ± 3.84	27.9 ± 4.1	27.6 ± 5.7
Duration of infertility (m)			
Baseline	21.30+1.07	21.9+1.42	21.60+1.65
Systolic BP (mmHg)			
Baseline	111.2 ± 9.5	135 ± 10.3	125.2 ± 12.4
Diastolic BP (mmHg)			
Baseline	71.7 ± 13.7	85.7± 11.4	76.6± 11.8
VO2 max (ml/kg*min)			
Baseline	32.44 ± 4.22	35.4 ± 3.9	38.4 ±4.1
BMI (Kg/m2)			
Baseline	22.8 ± 2.3	33.45 ± 2.75	31.7± 3.8
3 weeks	22.2 ± 2.1*	31.9 ± 2.65* ¥	30.4 ± 2.9* ¥
12 weeks	21.8 ± 1.95*	28.5 ± 2.25* ¥	26.8 ± 2.54* ¥
BW			
Baseline	71.2 ±2.5	89.8 ± 6.95	84.9 ± 7.2
3 weeks	69.5 ± 1.7*	86.4 ± 6.72* ¥	82.9 ± 6.1* ¥
12 weeks	65.4 ±2.2*	84.8 ± 6.42* ¥	82.2 ±5.72* ¥
WC (cm)			
Baseline	75.2 ±3.7	96.2 ±3.52	94.2 ±3.82
3 weeks	73.5 ± 1.9*	94.5 ± 3.32* ¥	73.5 ± 1.9* ¥
12 weeks	72.7 ± 2.6*	93.8 ± 3.26* ¥	72.7 ± 2.6* ¥
WHR			
Baseline	0.69 ± 0.02	0.91+0.07	0.91+0.06
3 weeks	0.66 ± 0.04*	0.89 ± 0.08* ¥	0.90 ± 0.04* ¥
12 weeks	0.60 ± 0.06*	0.80± 0.09* ¥	0.86±0.03* ¥
Ferriman–Gallwey score (hirsutism score)			
Baseline	5.34 ± 2.58	12.8 ± 3.67	11.6 ± 2.98
3 weeks	5.25 ± 2.47*	12. 65± 2.56* ¥	11.2 ± 2.87* ¥
12 weeks	5.22 ± 2.45*	12.61 ± 2.48* ¥	10.89 ± 2.65* ¥

Values are expressed as mean ±standard deviation

*P , 0.05 versus baseline. ¥ P , 0.05 versus Group A

BW: Body weight. WC: Waist circumference. WHR: Waist-to-hip ratio. BP: Blood pressure. BMI: Body mass index. VO2: Maximal oxygen consumption. PCOS: Polycystic ovary syndrome.

Table-2: Biochemical data at baseline and at 3- and 12-week supervised aerobic training follow-ups of obese women with or without polycystic ovary syndrome (PCOS).

Parameters	Group A (Control; n=30)	Group B (PCOS; n=30)	Group C (Obese; n=30)
FSH (mIU/ml)			
Baseline	6.94 ± 2.96	6.8+3.78	5.87 ± 4.8
3 weeks	7.8 ± 2.78*	7.6 ± 3.62*¥	6.4 ± 4.5*¥
12 weeks	8.6 ± 2.56*	8.2 ± 2.94*¥	7.5 ± 3..5*¥
E2 (pmol/l)			
Baseline	38.7 ±16.8	126.5 +21.6	35.61± 14.8
3 weeks	41.9 ±17.8*	121.3 +18.9*¥	38.82± 12.8*¥
12 weeks	46.92 ±12.9*	98.6 +16.7*¥	46.9 ± 9.8*¥
PRL (ng/ml)			
Baseline	8.5 ± 5.45	32.5 ± 7.8	21.5 ± 8.1
3 weeks	6.9 ± 4.25*	30.6 ± 6.4*¥	18.7 ± 7.2*¥
12 weeks	5.75 ± 3.82*	26.4 ± 5.3*¥	15.5 ± 5.8*¥
AMH (ng/ml)			
Baseline	2.83 ± 2.8	10.5 ± 3.56	4.6 ± 1.49
3 weeks	2.80 ± 2.76*	8.92 ± 3.23*¥	4.1 ±1.4*¥
12 weeks	2.84 ± 2.71*	6.52 ± 2.95*¥	3.6 ± 1.5*¥
Adiponectin (ng/ml)			
Baseline	12.8 ± 1.6	5.8 ± 1.3	6.4 ± 2.6
3 weeks	12.9 ± 1.8*	6.4 ± 1.7*¥	7.2 ± 2.9*¥
12 weeks	13.5 ± 1.5*	8.9 ± 2.5*¥	8.6 ± 3.2*¥
Fasting glucose (mg/dl)			
Baseline	107.5 ± 23.9	115.2±70.2	133.2 ± 69.48
3 weeks	72.36 ± 28.8*	106.2 ± 59.4*¥	109.8 ± 49.32*¥
12 weeks	68.4 ± 16.2*	81 ± 50.4*¥	100.8 ± 28.26*¥
Fasting insulin (mU/ml)			
Baseline	11.7±3.4	17.8±4.20	20.6 ± 8.2
3 weeks	9.8 ±4.37*	16.3± 3.9*¥	18.9 ± 6.95*¥
12 weeks	9.1±2.2*	14.8± 2.9*¥	16.1 ± 5.1*¥
GIR			
Baseline	5.66 ± 2.8	4.66 ± 3.91	3.98± 2.5
3 weeks	7.9 ± 1.82*	5.9 ± 3.95*¥	4.9 ± 3.1*¥
12 weeks	10.2 ± 1.7*	6.3 ± 3.85*¥	5.4 ± 3.5*¥
HOMA-IR			
Baseline	1.22 ± 0.57	1.24 ± 0.38	1.35 ± 0.49
3 weeks	1.18 ± 0.35*	1.18± 0.59*¥	1.28 ± 0.32*¥
12weeks	1.13 ± 0.25*	1.10 ± 0.42*¥	1.16 ± 0.22*¥
AFC			
Baseline	8.6± 6.2	21.6 ± 6.4	5.9 ± 4.3
3 weeks	8.9 ± 5.8*	20.0 ± 5.2*¥	6.3 ± 4.6*¥
12 weeks	9.1 ± 6.2*	14.7 ± 5.8*¥	7.1 ± 4.3*¥

FSH: Follicle -stimulating hormone
PRL: Prolactin
E2: Oestrogen
GIR: Fasting glucose-to-insulin ratio
HOMA-IR: Homeostasis model of assessment of insulin resistance
PCOS: Polycystic ovary syndrome
AFC: Antral follicle count
AMH: Anti-Müllerian hormone
*P , 0.05 versus baseline, ¥P , 0.05 versus Group A.

The mean age was 28.7±3.84 years in group A, 27.9±4.1 years in group B and 27.6±5.7 in group C.

Twelve weeks of moderate aerobic training produced a significant effect on clinical, anthropometric and biochemical characteristics among the participants. Anthropometric data obtained such as BMI, BW, WC and WHR were reduced significantly ($p<0.05$) in group B and group C when compared with their respective baselines and group A, respectively. For instance, the mean BMI among groups A, B and C was 22.8±2.3 kg/m^2, 33.45±2.75 and 31.7±3.8, respectively, at enrolment compared to 21.8±1.95, 28.5±2.25 and 26.8±2.54 after 12 week (Table-1).

Hormonal and biochemical measures including PRL, fasting blood glucose, fasting insulin (FI), and HOMA-IR were significantly lower by 12 weeks of moderate aerobic training in group B ($p<0.05$) and group C ($p<0.05$) compared to group A or their respective baseline values. At the same time, FSH, E2, GIR and adiponectin were significantly higher ($p<0.05$), and AMH levels were significantly lower ($p<0.05$) in PCOS and obese women following 12 weeks aerobic training compared to control group or their respective baselines. There was significant increase ($p<0.05$) in AFC for obese and control groups compared to PCOS women with significant reduction in AFC count (Table-2).

There was significant correlation between the change in BMI, blood glucose, FI, HOMA-IR, FSH, PRL and E2 and the improvement in AFC, ovarian volume, and hirsutism score towards AMH and adiponectin serum levels of responder group compared to non-responders (Table-3).

There were 30(33.3%) participants in the responders group, including 20(66.7%) obese and 10(33.3%) PCOS patients. Similarly, there were 30(33.3%) non-responders, including 20(66.7%) PCOS and 10(33.3%) obese patients.

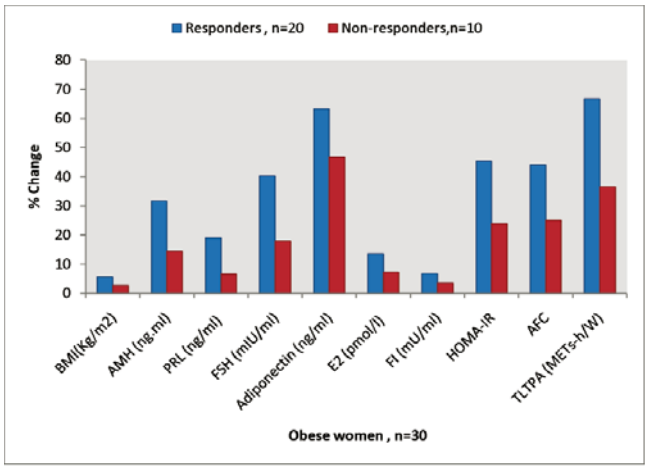
In the responders group, women showed significant improvements in reproductive functions such as increase in ovulation rates and improve in menstrual cyclicity. Also, 8(26.7%) women had enhancement in ovulatory and menstrual cyclicity (4(50%) amenorrhoeic women regained a cycle, 3(37.5%) improved cycle length variation and 1(12.5%) improved cycle length); 17(56.7%) women showed an improvement in menstrual cyclicity (9(52.9%) with regular cycles, 5(29.4%) with improving in cycle length, and 3(17.6%) with improving in cycle length variation); and 5(16.7%) women showed an improvement in ovulation.

The change in anthropometric, hormonal, and clinical data was significantly correlated in patients who responded to the improvement in reproductive function.

Table-3: Correlation analysis of clinical, hormonal, and ultrasonographic parameters in the PCOS and obese groups according to the levels of AMH and adiponectin (n=60).

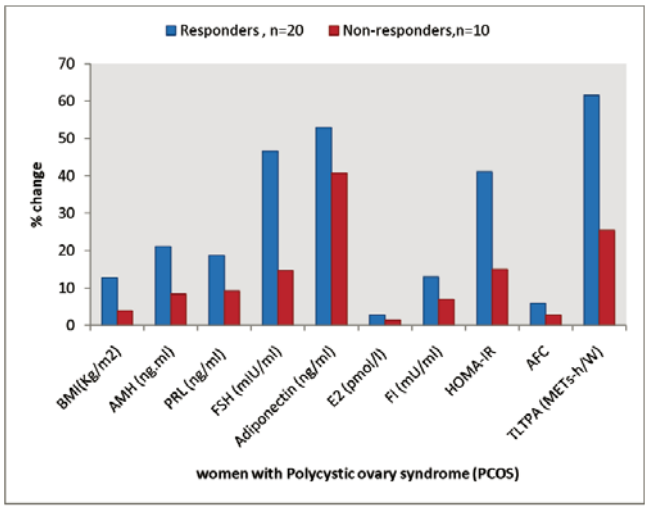
Parameters	Responders (n=30)				Non -responders (n=30)			
	Obese (n=20)		PCOS (n=10)		Obese (n=10)		PCOS (n=20)	
	AMH	Adiponectin	AMH	Adiponectin	AMH	Adiponectin	AMH	Adiponectin
BMI(Kg/m^2)	- 0.086 * *	- 0.095 * *	- 0.213 * *	- 0.198 * *	- 0.045 *	- 0.078 *	- 0.325 *	- 0.267 *
PRL (ng/ml)	- 0.367 *	- 0.176 *	-0.421 *	- 0.285 *	-0.512 *	- 0.380 *	-0.145 *	- 0.168 *
FSH (mIU/ml)	-0.358 *	- 0.156 *	-0.143 *	- 0.125 *	-0.347 *	- 0.196 *	-0.250 *	- 0.557 *
E2 (pmol/l)	- 0.085 *	- 0.074 *	- 0.095 *	- 0.082 *	- 0.065 *	- 0.056 *	- 0.112 *	- 0.134 *
FI (mU/ml)	-0.114 *	-0.117 * *	-0.121 *	-0.125 *	-0.132	-0.127 *	-0.132 *	-0.148 *
HOMA-IR	-0.096 *	-0.230 * *	-0.110 * *	-0.143 * **	-0.052 *	-0.132 *	-0.075 *	-0.137 *
AFC	0.627 * *	0.542 * *	0.357 * *	0.420 * *	0.475 *	0.320 *	0.316 *	0.685 *
Ovarian volume	0.128 * *	0.327 * *	0.460 * *	0.532 * *	0.325 *	0.580 *	0.384 *	0.642 *
TLTPA (METs-h/W)	0.135 * *	0.362 * *	0.284 * *	0.278 * *	0.265 *	0.297 *	0.145 *	0.165 *
Hirsutism score	0.085 *	0.096 *	0.28 *	0.078 *	0.065 *	0.097 *	0.045 *	0.065 *

BMI: Body mass index
PRL: Prolactin
FSH: Follicle -stimulating hormone
E2: Oestrogen
FI: Fasting insulin
HOMA-IR: Homeostasis model of assessment of insulin resistance
AFC: Antral follicle count
TLTPA: Total leisure time physical activity
METs-h/W: Metabolic equivalents hours per week
AMH: Anti-Müllerian hormone
PCOS: Polycystic ovary syndrome
Data presented as coefficient (R); * denotes significance at <0.05; ** denotes significance at <0.01.



BMI: Body mass index
AMH: Anti-Müllerian hormone
PRL: Prolactin
FSH: Follicle -stimulating hormone
E2: Oestrogen
FI: Fasting insulin
HOMA-IR: Homeostasis model of assessment of insulin resistance
AFC: Antral follicle count
TLTPA: Total leisure time physical activity
METs-h/W: Metabolic equivalents hours per week

Figure-1: Percent change in BMI, physical activity, fertility hormones, and reproductive functions among obese women following 12 -weeks of supervised aerobic exercise.



BMI: Body mass index. AMH: Anti-Müllerian hormone.
PRL: Prolactin
FSH: Follicle -stimulating hormone
E2: Oestrogen
FI: Fasting insulin
HOMA-IR: Homeostasis model of assessment of insulin resistance
AFC: Antral follicle count
TLTPA: Total leisure time physical activity
METs-h/W: Metabolic equivalents hours per week.

Figure-2: Percent change in BMI, physical activity, fertility hormones, and reproductive functions among women with Polycystic ovary syndrome (PCOS), following 12 -weeks of supervised aerobic exercise.

In the responders group, there was a significant reduction in BMI, AMH, PRL, FI, HOMA-IR, whereas FSH, E2, adiponectin level and AFC count were significantly higher compared to the non-responders group. The obtained data was confirmed with higher significant rate ($p< 0.01$) of leisure-time physical activity (LTPA) in responders compared to non-responders (Figures-1 and 2).

Discussion

Recently, women infertility has been faced with more challenges in medicine. PCOS is the most common endocrine abnormality causing infertility in premenopausal women.[28] Previously, clinical treatment trials showed that optimising of healthy weight, improving underlying hormonal disturbances, prevention of future reproductive disorders and improving quality of life increase the rate of fertility among PCOS patients.[29]

Metabolic disturbances, such as insulin resistance and obesity are also associated with PCOS. It is thought to have a genetic aetiology. The severity and course of the disease are determined by lifestyle changes, especially BMI.[30] Lifestyle (dietary, exercise or both) interventions are recommended as first-line treatment methods in an international position statement on PCOS. Overall, the use of lifestyle interventions are preferable and cost-effective initial treatment strategy,[2] compared to surgical and pharmacological options.[3,17,18] Improvement of lifestyle of women with PCOS helps in prevention of excess weight gain, future reproductive and metabolic complications especially those with a greater incidence of overweight and obesity compared to the general population.[31,32]

Studies on lifestyle behaviours showed that the increase in physical activity and a reduction in caloric intake significantly improve ovulatory function, circulating androgen levels, inflammatory pattern, and insulin sensitivity in women with PCOS.[17-20] Therefore, there is a strong rationale for lifestyle interventions for both improving underlying hormonal imbalances and management of weight for a large proportion of women with PCOS. In this study, we evaluated the association between physical activity and fertility status in women with obesity and PCOS following SAE interventions for 12 weeks. The clinical efficacy of the lifestyle interventions depends mainly up on several clinical and hormonal factors to improve the fertility status in women with PCOS.[33]

In the present study, we attempted to characterise the mechanisms that underlie the efficacy of SAE in the restoration of ovarian function in obese and PCOS patients. Both 3 and 12 weeks' interventions induced improvements in BW, BMI, WHR, WC within 12 weeks. Previous studies have suggested that weight loss, even though minimal, could be the main factor involved in the restoration of fertility.[1,34,35] The significant improvement in WC after 3 and 12 weeks of SAE interventions suggests a potential role of visceral fat reduction in enhancing ovulation. The change in visceral fat in response to lifestyle modification ultimately reduces androgens and insulin resistance independently of BW. Some papers indicated that physical activity has been found lower in PCOS patients than in control women.[1,36] The changes in lifestyle that incorporate an increase of physical activity and limited caloric intake have been beneficial in some studies. PA can improve body composition, glucose homeostasis and insulin sensitivity.[37]

Exercise-induced weight loss has been shown to improve metabolic function and hormonal profiles, and often leads to significant increase in fertility.[38]

We evaluated the main clinical and biochemical data at baseline, and after 3 and 12 weeks of SAE intervention to elucidate potential mechanisms of ovarian sensitisation to SAE. We observed a reduction in PRL and an improvement in serum FSH, E2, blood sugar, insulin levels, GIR and HOMA-IR. The data was in accordance with other research studies on human and animal models which represent a significant improvement in FSH, luteinising hormone (LH), androstenedione, oestrogen levels, and insulin sensitivity following exercise interventions of medium and moderate intensity, and subsequently an improvement in the symptoms of ovarian disorders was reported among females with PCOS. The mechanism by which exercise can improve ovarian functions may be by reduction in body weight and fats in women with PCOS whereas oestrogen is stored and steroid hormones are produced and subsequently an increase in ovarian hormones.[39-42]

This study discussed the relation between AMH hormone and adiponectin levels. There was significant decrease in AMH and increase in adiponectin levels in obese and PCOS female patients. Our data shows that there is an inverse relationship between AMH hormone and adiponectin levels and the improvement in BMI, fertility hormones; FSH, E2, PRL and metabolic disorders; fasting glucose, insulin, GIR and HOMA-IR following 12 weeks SAT interventions. The data conformed to the findings of Barr et al.,[43] who reported the importance of dietary intakes and levels of physical activity that optimise symptom management and disease prevention among women with PCOS.

Several reports also indicate that the basal serum levels of AMH are more discriminatory markers of the ovarian

response than the basal FSH, inhibin B or oestradiol.[44] The level of AMH plays a significant role in women fertility whereas high concentrations of AMH affect FSH responsiveness, steroidogenesis and the acquisition of the LH receptors in the small antral follicles. However, by the time the inter cycle rise in the FSH occurs, the AMH production would cease, the concentrations would fall and the follicle would be 'released' to produce oestradiol. This normal mechanism is changed in patients with PCOS, which is attributed to higher AMH production.[45,46] So, in our study the effect of moderate physical exercise reduced the body fat where oestrogen is stored and steroid hormones are produced,[46,47] which in turn increased FSH and decreased the level of AMH.

Regarding the role of adiponectin in fertility of obese and PCOS women following 12-week SAT, adiponectin levels were found to be lower in women with obesity and/or PCOS. Adiponectin levels were related to insulin sensitivity: insulin and glucose levels which are often measured in PCOS in combination with BMI correlate, as expected, with lower adiponectin level. The more insulin-resistant patients had lower adiponectin levels. As mentioned above, it is possible that lower levels of adiponectin may contribute to the increased levels of LH observed in some women with PCOS.[47] In addition, Caminos et al.[48] reported that in vitro conditions, adiponectin-hormone opposing insulin resistance secreted from fat cells tackles secretion of testosterone and has an important role in raising sensitivity to insulin and androgens. In a study done by Wang et al.,[49] a decline in adiponectin quantities in PCOS women is seen. Different studies have shown that the long sport activity can cause a rise in adiponectin amounts and a decline in leptin amount.[50,51]

Therefore, probably increasing adiponectin quantities and decreasing leptin quantities resulting from sport activity are some of the other mechanisms for decreasing anderogen quantities and improving insulin sensitivity following sport activity.[52] The relationship of female fecundity biomarkers such as AFC, ovarian volume and hirsutism score with AMH hormone and adiponectin levels was evaluated in obese and PCOS patients. There was significant improvement in AFC count, ovarian volume and hirsutism score within obese and PCOS patients following 12 weeks SAT interventions. The improvement in AFC count, ovarian volume and hirsutism score was significantly correlated with the increase in adiponectin and decrease in AMH hormone levels in obese and PCOS patients.

AMH and AFC have been shown to be the most sensitive ones for assessment of ovarian reserve in these studies. AFC and ovarian volume provide direct measurements of ovarian reserve, while AMH is released from growing follicles and so its level reflects the size of developing follicle cohort.[53,54]

The highest level of AMH expression is present in granulosa cells of secondary, pre-antral and small antral follicles up to 6mm in diameter,[54] therefore, level of AMH may represent the population of these follicles. More studies reported that both AMH and AFC are accurate predictors of excessive response to ovarian hyper stimulation.[55] Also, it has been shown that AMH has at least the same level of accuracy and clinical value for the prediction of poor response and non-pregnancy as AFC.[56] Recently, it was reported that AFC and AMH correlate with each other but have independent significance for estimating follicles >12 mm on day of human chorionic gonadotropin (hCG).[57]

Regarding the effect of physical activity following 12 weeks' SAT interventions, positive activity impact was reported on ovarian reserve markers in both normal, obese and PCOS reproductive age women, though this was more pronounced and statistically significant only in case of PCOS and obese women. The data is in agreement with many recent studies which reported positive impact of physical activity on ovarian reserve markers and fertility outcomes in reproductive age women,[28,50-58] and inconsistent with other studies which reported that vigorous physical activity was associated with negative impact on fertility outcomes; but again this was attributed to negative energy balance in these women rather than physical activity.[59]

Regarding adiponectin, positive impact with fertility biomarkers was reported in obese and PCOS women of this study, whereas adiponectin influenced gonadotropin release, normal pregnancy and assisted reproduction outcomes. Higher levels of adiponectin were associated with improved menstrual function and better outcomes in assisted reproductive cycles.[60]

Improvement in menstrual function and assistance of reproductive cycles were reported in obese women with PCOS via a reduction in adiposity, increase in the levels of adiponectin, and decrease in AMH levels following 12 weeks of SAE of moderate intensity.

In particular, an improvement in ovarian reserve was reported with an ovulation rate of 43.3% and a restoration of menstrual cycle in 56.7% of patients who were previously anovulatory.

The small sample size was a limitation of this study.

Conclusion

Moderate aerobic training for 12 weeks had a positive significant effect in improving reproductive functions via modulating adiposity, the levels of adiponectin, AMH and fertility hormones of obese infertile women with PCOS. Also, adiponectin and AMH could be useful as markers for the prediction of ovarian response to non-drug exercise interventions.

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