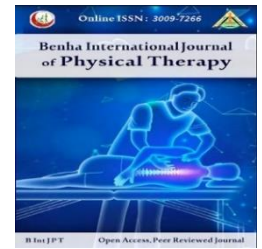


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Original research

Effect of cryolipolysis on hormonal profile and menstrual regulation in obese women with polycystic ovarian syndrome

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Abstract

Background: Polycystic ovarian syndrome (PCOS) is a frequent disease in women that affects their ability to reproduce, their metabolism, and their ability to control their androgen levels. It is brought on by an imbalance of female sex hormones as well as being aggravated by obesity. **Purpose:** To examine the effects of cryolipolysis on hormonal profile and menstrual regularity in obese women with PCOS. **Methods:** 50 female patients, aged from 18 to 30 years, were split into two groups of 25 patients each at random. Group A (control group), treated by a diet regime and aerobic exercise for 12 weeks; Group B (study group): treated by the same diet regime and aerobic exercise as Group A in addition to cryolipolysis for 45 minutes per session, every 2 weeks for 12 weeks. Assessment of all females was carried out through measuring weight, body mass index (BMI), waist hip ratio, luteinizing hormone (LH), follicle-stimulating hormone (FSH), and insulin resistance (IR), in addition to menstrual regularity pre- and post-treatment. **Results:** There was a significant improvement ($P < 0.05$) in all measured variable after treatment compared to before treatment in both group A and B, by comparing post treatment values there is a significant difference ($p < 0.05$) in all measured variable favouring the study group (group B). **Conclusions:** Cryolipolysis in addition to diet regime and aerobic exercise has significant effect on hormonal profile as well as menstrual regularity in obese women suffering from PCOS. **Keywords:** Cryolipolysis, Hormonal Profile, Menstrual Regulation, Obese Women, Polycystic Ovarian Syndrome.

Introduction

Polycystic ovary syndrome (PCOS) is a highly heterogeneous condition and the most prevalent endocrine-metabolic disorder affecting reproductive-age women. Its most common symptoms include irregular menstrual cycles, secondary amenorrhea, elevated testosterone levels, ovarian cysts detected by ultrasound, hirsutism, acne, obesity, as well as infertility. Worldwide, it impacts 5-20% of reproductive-age women.¹

Anovulations along with infertility are symptoms of PCOS, which is caused by an imbalance between the hypothalamus-hypophysis axis and elevated levels of androgenic hormones.²

Endometrial cancer, hyperlipidaemia, obesity, hypertension, heart disease, diabetes mellitus (DM), as well as pregnancy-associated diabetes are among the long-term complications that can develop from PCOS.³

Recent genetic investigations have confirmed the strong association between obesity and PCOS shown in epidemiological studies. Obesity and weight increase contribute to PCOS through a variety of mechanisms. Important processes include the metabolic consequences of insulin resistance (IR) and the steroidogenic and reproductive consequences resulting from hyperinsulinemia. The core pathogenesis of PCOS has thus been IR.⁴ PCOS frequently manifests with obesity-related low-grade inflammation.⁵

Glucose intolerance and IR are two symptoms of PCOS, and reducing weight may alleviate these problems. About half of women with PCOS have reported a marked improvement in menstrual cycle abnormalities and ovulation after performing exercise training. The amplitude of the luteinizing hormone pulse may decrease as weight reduction progresses, leading to a decrease in androgen production.⁶

The gold standard for body shaping has long been liposuction.⁷ However, cryolipolysis was created to perform adipocyte damage due to the higher risk of problems and other problems associated with this method.⁸ Another non-invasive option for body shaping is cryolipolysis.⁹ The purpose of this study was to determine whether cryolipolysis improved hormonal profile as well as menstrual regularity in obese women, also we hypothesized that cryolipolysis in addition to diet regime and aerobic exercise has a positive effect on hormonal profile as well as menstrual regularity in obese women suffering from PCOS.

Methods

Ethical consideration:

The Ethics Review Committee of Cairo University's Faculty of Physical Therapy, Egypt gave its approval to the project with ethical approval no (REC/022/004763). It was also prospectively registered at clinical trials government (NCT 06226701). This study was carried-out from September 2023 to January 2024 at the Outpatient Clinic of Elzawamal Central Hospital at ElSharqia, Egypt.

Participants

Fifty women diagnosed as having PCOS by their gynaecologist were recruited from the outpatient clinic of Elzawamal Central Hospital at El-Sharqia, Egypt. Women who fulfilled the

following criteria were allowed to take part in the study: they had to be between the ages of 18 to 30 years old, their BMI was above 25kg/m² and less than 35kg/m², their waist /hip ratio was >0.9 cm, had irregular menstrual cycle (less than 21 day per month or more than 35 day /month for more than 3 months). Women weren't allowed to participate if they had thyroid disorders, hepatic diseases, bleeding disorders, cardiovascular and respiratory disease, malignancy, renal failure, recent operation, pacemakers or surgical implantations, and Raynaud's disease (uncommon disorder characterized by cold temperature can reduce blood circulation to the digits).

Study design:

This study was a single blinded randomized control study. All women were randomized into two groups equivalent in number, using selected envelope method. Group A: consisted of 25 women, they were treated by 1200cal /day diet regime and aerobic exercise for 3 months. Group B (study group): consisted of 25 women, they were treated by 1200cal/day diet regime, aerobic exercise and cryolipolysis for 45 m/session, session every 2weeks for 3months.

Procedures:

Firstly, before starting the study, all female were instructed about assessment and treatment procedures to gain their cooperation and confidence. After each participant was given a thorough explanation of the study's purpose, methods, and potential benefits, as well as their rights to withdraw from participation at any moment without prejudice, they were asked to sign an informed consent form.

Evaluation procedure:

Weight and body mass index:

Weight and height were measured for each women in both group A and B before and after the treatment to calculate the BMI according to the following equation $BMI (kg/m^2) = \text{weight (kg)} / \text{Height (m}^2\text{)}$.¹⁰

Waist/ hip ratio:

From standing position with both feet together, waist circumference was assessed around the midpoint among iliac crests and lower rib margins after normal expiration, while the hip

circumference was assessed at the level of greater trochanter. Calculation of waist/hip ratio was done for each woman by dividing waist circumference by hip circumference. ¹¹

Hormones levels (LH/FSH ratio and IR)

A sample of venous blood was drawn from each woman at the 2nd or 3rd day of the menstrual cycle. Lab analysis was done to detect the level of reproductive hormones (luteinizing hormone, follicle-stimulating hormone and luteinizing hormone/follicle-stimulating hormone ratio) and IR before and after three months. The blood analysis was done at the laboratory of Zagazig General Hospital at El-Sharqia, Egypt. Normally LH/FSH ratio is about 1:1 therefore, in young fertile women, the levels of FSH and LH are frequently both within the range of around 4-8. Although LH levels are typically 10–20, FSH levels in PCOS women are additionally in the 4–8 range.¹²

Menstrual regularity:

All women noted their menstrual cycle for 3 months during treatment and follow up for another 3 months by menstrual calendar. The regularity of the menstrual cycle was recorded as: 28 days, fewer or more than 28 days. ¹³

Treatment Procedures:

Group A (control group)

Each female in group A followed diet regime with 1200 cal./day, diet regime was changed every week as well as a program of aerobic exercise (session lasted for 25 minutes, 3 sessions per week for 3 months). There were three stages to the exercise protocol that occurred throughout each session: A three-minute warming up to facilitate the variety of physiological changes that must occur before exertion.

The conditioning component of the exercise program consists of an aerobic exercise period lasting 20 minutes at an intensity level of 50-60% of maximum heart rate. During the two-minute cooling down, keep the muscles engaged to keep venous return so that blood doesn't pool in the extremities. Utilizing the Karvonen heart rate reserve model, the exercise training intensity that was advised for the main phase was: Calculator for indicator heart rate: subtract resting heart rate from

maximum heart rate, multiply by intensity training, and add resting heart rate. ¹⁴

Group B (study group)

Each female in group B followed the identical program as in group A in addition to cryolipolysis for 45 min/session every 2 weeks for 3 months. Fat lipolysis was carried out using the A1 max cool shaping equipment, which is an informant of China Korean Technology. To prevent bruising or ecchymosis, the device's cooled gel pad should be adhered to the treatment region before using the cool sculptor application head. A patient's tolerance level determines the optimal vacuum suction setting for this device. Woman assumed the supine lying position. The pad gel was put adherent to the lower abdomen, then the cool sculptor head and the device was turned on.

The intensity increases gradually until patient sense squeezing. The cooling temperature was adjusted according to the woman's tolerance and the release time was 1second. After ending the time, the device was turned off automatically. Following the session, the treated area was massaged for 5min using manual massage to increase the efficiency of cryolipolysis management. ¹⁵

Sample size calculation:

Software developed by Heinrich-Heine-University in Düsseldorf, Germany, known as G*power, version 3.1, was used to determine the study's sample size. For an overall of 46 individuals, we used F tests (MANOVA: Special effects as well as interactions) to calculate the sample size. The Type I error (α) was set at 0.05, the power (1- β error probability) was 0.90, the effect size f^2 (V) was 0.296584213, and the Pillai V was 0.4574855. This was done for two independent group comparisons and seven major variable outcomes. A minimum of 50 participants, with 25 patients in every group, is required for this study to account for a 10% dropout rate.

Statistical analysis:

Data were examined for tests of normality as well as homogeneity of variance. After removing outliers found via box and whiskers plots, the data was normalized using the Shapiro-Wilk test, which indicates that the data follows a normal distribution. There was also no statistically significant difference when tested for homogeneity

of variance using Levene's test. Parametric analysis is performed on normally distributed data.

The statistical analysis was carried-out utilizing statistical SPSS Package program version 25 for Windows (SPSS, Inc., Chicago, IL). Quantitative data for obese females with PCOS demographic data (age, weight, height, as well as BMI), body measurements (weight, BMI, and waist hip ratio), laboratory hormonal profile measurements (FSH, LH, LH/FSH, and IR) are reported as mean and standard deviation.

Chi-square test utilized to compare within and between groups for assessment of menstrual regularity. Mixed design 2 x 2 MANOVA was employed for the 1st independent variable with two levels (study group vs. control group) referred to the tested group, while the 2nd independent variable with two levels (pre-treatment vs. post-treatment) was the measurement period. The primary outcome measures were the body as well as laboratory hormonal profile measurements. When the MANOVA test found a statistically significant F value for one of the investigated variables, we utilized the Bonferroni adjustment test to compare the two sets of data within and across the groups. At the 0.05 level of probability, all statistical analyses were considered significant.

Results

The results of clinical general demographic data showed that no significant differences in mean values of PCOS females age (P=0.353), weight (P=0.629), height (P=0.905), and BMI (P=0.893) among study group and control group. (Table 1)

Table 1. Clinical general characteristics for participant's PCOS females in both groups

Items	Groups (Mean ±SD)		P-value
	Study group (n=25)	Control group (n=25)	
Age (yr)	25.72 ±2.68	25.00 ±2.76	0.353
Weight (kg)	82.24 ±6.77	82.04 ±5.07	0.629
Height (cm)	161.28 ±3.96	163.92 ±2.92	0.905
BMI (kg/m ²)	31.60 ±1.77	30.56 ±1.74	0.893

Data are reported as mean ±standard deviation. P-value: probability value P-value > 0.05: non-significant

Statistical multiple pairwise comparison tests for body measurement variables (weight, BMI, and waist hip ratio) within each group (Table 2) revealed that there was significant decline in weight within study group (P=0.0001), BMI (P=0.0001), and waist hip ratio (P=0.0001) post treatment in comparison with pre-treatment. Moreover, in control group, that there was significant decline in weight (P=0.013), BMI (P=0.002), as well as waist hip ratio (P=0.0001) after-treatment in comparison with before-treatment. The females with PCOS who treated by diet regime, aerobic exercise, and cryolipolysis for 3 months program (study group) improved weight, BMI, and waist hip ratio decreasing percentage (16.00, 16.04, and 28.30%, respectively) than females with PCOS (5.17, 5.30, and 14.56%, respectively) who treated by diet regime, aerobic exercise only for 3 months program (control group).

Statistical multiple pairwise comparison tests for body measurement variables (weight, BMI, and waist hip ratio) among both groups (Table 2) revealed that no significant differences have been detected before-treatment in weight (P=0.905), BMI (P=0.893), as well as waist hip ratio (P=0.291). At after-treatment, there were significant difference (P<0.05) in weight (P=0.0001), BMI (P=0.0001), and waist hip ratio (P=0.0001) between study group and control group. Moreover, this significant decline in weight, BMI, as well as waist / hip ratio at after-treatment is favourable in obese females with PCOS in study group than obese females in control group.

Statistical multiple pairwise comparison tests for laboratory measurement variables (FSH, LH, LH/FSH ratio, and IR) within each group (Table 3) revealed that there was significant rise in FSH (P=0.0001) post treatment in comparison with pre-treatment within study group, but there was insignificantly increased in FSH (P=0.868) after-treatment compared to before-treatment within control group. There were significantly decreased within study group in LH (P=0.0001), LH/FSH ratio (P=0.0001), and IR (P=0.0001) post treatment in comparison with pre-treatment.

Moreover, in control group, there were significant decline in LH (P=0.004), LH/FSH ratio (P=0.005), and IR (P=0.016) post treatment in comparison with pre-treatment. The females with PCOS who treated by diet regime, aerobic exercise, and cryolipolysis for 3 months program (study

group) improved FSH, LH, LH/FSH ratio, and IR percentage (16.96, 41.83, 51.47, and 29.06%, respectively) than females with PCOS (0.72, 11.04, 13.30, and 13.21%, respectively) who received the same diet regime, aerobic exercise only for 3 months program (control group).

Statistical multiple pairwise comparison tests for laboratory measurement variables (FSH, LH, LH/FSH ratio, and IR) among both groups (Table 3) revealed that no significant differences have been detected ($P > 0.05$) before-treatment in

FSH ($P = 0.765$), LH ($P = 0.697$), LH / FSH ratio ($P = 0.951$), as well as IR ($P = 0.991$). At after-treatment, significant differences in FSH ($P = 0.0001$), LH ($P = 0.0001$), LH / FSH ratio ($P = 0.0001$), and IR ($P = 0.004$) were found between study group and control group. Moreover, this significant increase in FSH and decrease in LH, LH/FSH ratio, and IR at after-treatment is favourable in obese females with PCOS in study group than obese females in control group.

Table 2: Within and between groups comparison for body measurements

Variables	Items	Groups (Mean \pm SD)		Change	P-value
		Study group (n=25)	Control group (n=25)		
Weight (Kg)	Before-treatment	82.24 \pm 6.77	82.04 \pm 5.07	0.20	0.905
	After-treatment	69.08 \pm 5.32	77.80 \pm 6.31	8.72	0.0001*
	Change (MD)	13.16	4.24		
	Improvement %	16.00%	5.17%		
	95% CI	9.84 – 16.47	0.92 – 7.55		
	P-value	0.0001*	0.013*		
Body mass index (BMI)	Before-treatment	31.60 \pm 1.77	30.56 \pm 1.74	1.04	0.893
	After-treatment	26.53 \pm 1.52	28.94 \pm 2.26	2.41	0.0001*
	Change (MD)	5.07	1.62		
	Improvement %	16.04%	5.30%		
	95% CI	4.03 – 6.10	0.58 – 2.66		
	P-value	0.0001*	0.002*		
Waist hip ratio	Before-treatment	1.06 \pm 0.06	1.03 \pm 0.07	0.03	0.291
	After-treatment	0.76 \pm 0.09	0.88 \pm 0.02	0.12	0.0001*
	Change (MD)	0.30	0.15		
	Improvement %	28.30%	14.56%		
	95% CI	0.24 – 0.36	0.09 – 0.21		
	P-value	0.0001*	0.0001*		

Data are reported as mean \pm standard deviation (SD)

MD: Mean difference CI: confidence interval P-value: probability value * Significant ($P < 0.05$)

Statistical analysis comparison between before- and after menstrual regularity distribution within each group (Table 4) showed that there was significant difference ($P < 0.05$) in frequency distributions among before- and after-treatment of menstrual regularity ($P = 0.003$) within study group. However, no significant difference ($P > 0.05$) in frequency distributions among before- and after-treatment of menstrual regularity ($P = 0.642$) within control group.

Statistical analysis comparison between both groups at before- and after menstrual regularity distribution (Table 4) showed that no significant difference ($P > 0.05$) at before-treatment of menstrual regularity distributions ($P = 0.916$) among study group as well as control group. But a significant difference was found ($P < 0.05$) at after-treatment of menstrual regularity distributions ($P = 0.031$) among study group and control group.

Table 3: Within and between groups comparison for laboratory hormonal profile measurements

Variables	Items	Groups (Mean ±SD)		Change	P-value
		Study group (n=25)	Control group (n=25)		
FSH (mIU/mL)	Before-treatment	5.60 ±1.01	5.52 ±0.94	0.08	0.765
	After-treatment	6.55 ±0.54	5.56 ±0.78	0.99	0.0001*
	Change (MD)	0.95	0.04		
	Improvement %	16.96%	0.72%		
	95% CI	0.48 – 1.43	-0.51 – 0.43		
	P-value	0.0001*	0.868		
LH (mIU/mL)	Before-treatment	11.12 ±1.51	10.96 ±1.04	0.16	0.697
	After-treatment	6.47 ±1.78	9.75 ±1.31	3.28	0.0001*
	Change (MD)	4.65	1.21		
	Improvement %	41.83%	11.04%		
	95% CI	3.84 – 5.46	0.40 – 2.01		
	P-value	0.0001*	0.004*		
LH / FSH ratio	Before-treatment	2.04 ±0.41	2.03 ±0.34	0.01	0.951
	After-treatment	0.99 ±0.30	1.76 ±0.20	0.77	0.0001*
	Change (MD)	1.05	0.27		
	Improvement %	51.47%	13.30%		
	95% CI	0.85 – 1.22	0.08 – 0.44		
	P-value	0.0001*	0.005*		
Insulin resistance (mcu/ml)	Before-treatment	2.65 ±0.68	2.65 ±0.36	0.00	0.991
	After-treatment	1.88 ±0.55	2.30 ±0.30	0.42	0.004*
	Change (MD)	0.77	0.35		
	Improvement %	29.06%	13.21%		
	95% CI	0.48 – 1.04	0.06 – 0.62		
	P-value	0.0001*	0.016*		

Data are reported as mean ± standard deviation (SD)

MD: Mean difference CI: confidence interval P-value: probability value * Significant (P<0.05)

Table 4: Within and between groups comparison for menstrual regularity

Items	Categories	Study group (n=25)	Control group (n=25)	P-value
Pre-treatment	More than 28 days	16 (64%)	15 (60%)	0.916
	Within 28 days	6 (24%)	6 (24%)	
	Fewer than 28 days	3 (12%)	4 (16%)	
Post-treatment	More than 28 days	5 (20%)	13 (52%)	0.031*
	Within 28 days	18 (72%)	9 (36%)	
	Fewer than 28 days	2 (8%)	3 (12%)	
P-value		0.003*	0.642	

Data are expressed as frequency (percentage)

P-value: probability value S: significant * Significant (P<0.05) NS: non-significant

Discussion

PCOS is a common complain affecting 5–20% of women within the reproductive age around the world with the subsequent anovulation and therefore causing menstrual irregularity and in turn lead to infertility¹⁶. This study aimed to investigate the impact of Cryolipolysis on body measurement, hormonal profile, as well as menstrual regularity in obese women with PCOS

I. Body measurement including weight, BMI, and waist hip ratio

Our findings revealed that there was a significant improvement ($P \leq 0.05$) in body measurement including weight, BMI, and waist hip ratio in both groups with greater improvement in the study group than control group in post treatment comparison.

Regarding the significant improvement in the control group who treated by diet regime and aerobic exercise can be explained as following: restricting diet or calorie intake is associated with reduced adiposity and subsequent weight loss that had a significant effect on the glycemic index, metabolic health, and glucose homeostasis.¹⁷ As well, exercise experienced greater improvement in fat mass and reduced both subcutaneous and intra-abdominal body fat which decrease the waist hip ratio.¹⁸

The result of this study was supported by Hsu et al. who studied the impact of diet and exercise on metabolic function, physical performance, as well as body composition of those with mean sarcopenic obesity (SO). Results showed that physical performance, metabolic health, body composition, as well as BMI were all positively affected by dietary and activity changes.¹⁹

Results of the current study in the same line with Ukuar . who examined the impact of multi-strain probiotic accompanied by dietary and lifestyle adjustments on PCOS and concluded that they were effective in reducing weight, BMI, waist-hip ratio.²⁰

Regarding to the superior effect of cryolipolysis on the improvement in all body measurement variables including weight, BMI, waist-hip ratio can explained as cryolipolysis controlled cooling to freeze and crystallise fat under skin without damaging the surrounding muscle and skin tissue. This causes apoptosis (dead fat cells are processed and naturally eliminated by

the body through the liver and removed for good. Afterwards, the remaining cells in the treated area condense, leaving less fat, reduce both subcutaneous and intra-abdominal body fat which in result decrease weight, BMI, waist-hip ratio.²¹ Our, findings are in line with Ingargiola et al., who investigated the effects of cryolipolysis on contouring as well as loss of fat. they concluded that the procedure shows promise as a nonsurgical alternative to liposuction as well as other invasive techniques and that it is safe to employ for localized adipose tissues and has few side effects²². Similarly, Hwang et al. investigated the possibility that 12-week unilaterally cryolipolysis could alter visceral as well as subcutaneous adipose tissue, leading to an expected enhancement in metabolic function.²³

Our results were conflicted with falster who has mentioned that applying the cryolipolysis treatment once does not have a substantial impact on reducing the thickness of fat in the lower abdominal region of healthy women. This contradiction might be attributed to the low activity level of the participant at the study of Falster and his colleagues, however , Falster assessed the abdominal adiposity using ultrasound.²⁴

II. Hormonal profile

Reasons for the beneficial impact of exercise and diet on hormone profile include the fact that excess visceral fat is linked to IR, elevated insulin, along with Insulin-like Growth Factor 1 (IGF-1). To assist in the activation of LH receptors, sensitizing substances like insulin and IGF-1 improve the response of granular cells in small antral follicles to FSH. Furthermore, insulin and IGF-1 promote testosterone production in ovarian cells.²⁵ However, diet regime is associated with reduction of fat cell, BMI, waist/hip ratio so, improving the IR, hormonal profile, and metabolic profiles.²⁶ In addition, the hypothalamic-pituitary-ovarian axis (HPOA) interacts with hypothalamic endorphin, which reduces high sympathetic nerve activity, and exercise improve menstrual cyclicity, stimulate ovulation, reduce testosterone, insulin, LH, as well as the LH/FSH ratio; they achieve this by providing an atonic inhibitory impact on the Gonadotropin-releasing hormone (GnRH) generator in addition to the pituitary LH secretion.²⁷

Our results were supported by the findings of a study by Cowans who reported that combining

exercise and diet regime had a significant improvement in all measured outcomes including weight, BMI, waist circumference, body fat, fat free mass, glucose, insulin HOMA-IR, testosterone(T), Sex hormone-binding globulin (SHBG) and free Androgen Index (FAI).²⁸

As cryolipolysis has superior effect in reducing the visceral fat when combined by diet regime and aerobic exercise rather than diet and exercised alone so, it has superior effect in improving glycemic control, IR, which regulate level of androgen, LH, and FSH hormones. This finding are supported by Abdel-Aal et al. who showed that lipid profile, insulin, sex hormones, as well as liver enzyme elements were more improved in women who received cryolipolysis in addition to a diet program than in women who received diet program maintenance alone.²⁹

Our results about the effect of cryolipolysis on hormonal profile conflicted with Badran et al. who clarified that nonsurgical elimination of fat had long-lasting impacts on body measurements, that alterations in blood lipid profiles were temporary, and that there is now insufficient data to believe that nonsurgical fat elimination has metabolic benefits.³⁰

The contradiction of our result with that of Badran. May be due to lack number of session or different doses. Badran made his evaluation with in 60 days, he made it clear through them that changes in hormone profiles are temporary in the short term, but that there may be a metabolic benefit to removing too much ASF. However, he also recognized the need for well-conducted future clinical research and appropriately designed dose-response trials to determine whether this benefit lasts over the long term. This was in line with our study, which lasted for 3 months and our results followed up other 3 months again which made data more clear and significant.

III. Menstrual regularity

Regarding to positive effect of diet and exercise on menstrual regularity can be explained by: Both diet and exercise increase hypothalamic β -endorphin secretion and sympathetic nerve activity which decrease testosterone, LH/LFSH ratio and improved menstrual frequency which in turn increase the mean follicular size and improve the fertility. This fact supported by Hutchison et al. who examined the effect of exercise on IR as well as body composition in overweight along with

obese women with and without PCOS and reported that weight loss in obese and overweight women has a significant effect on fertility as well as triglyceride level improvement due to decrease in BMI, waist circumference, FSH, LH and improved menstrual cycle.³¹

Regarding the superior effect of cryolipolysis on menstrual regularity can explained by the greater decrease in IR and LH/FSH ratio that associated with greater improve in menstrual frequency and fertility. The follicular stage of the menstrual cycle is when ovarian follicles are stimulated to mature by FSH, just as they are by elevated levels of LH and FSH. A decrease in FSH secretion occurs when a dominant follicle begins secreting inhibin and estradiol. The hypothalamus releases an excess of GnRH in response to the dominant follicle's estradiol production, which must be sustained for at least 48 hours at a level of 200 to 300 pg/ml.³²

These results are supported by Beals who looked at collegiate athletes in the United States and found that many of them suffered from eating disorders, menstrual dysfunction, and poor bone mineral density. According to his findings, a healthy hypothalamic-pituitary-ovarian axis is necessary for a regular menstrual cycle.³³

Our results about the effect of Cryolipolysis on menstrual regularity conflicted with Costa et al. who explained that Cryolipolysis didn't alter body composition, lipid profile or inflammatory mediators studied, IR, and there was no effect on sex hormones and menstrual cycle.³⁴

Limitation

This study was limited to following criteria, all women's ages was ranged between 18 to 30 years old, their BMI was above 25kg/m² and less than 35kg/m², this study also limited by Cooperation of the women, it is affected the result of the study. Psychological status and Lack of Financial support.

Conclusion

The study results adding that cryolipolysis in addition to diet regime and aerobic exercise has effective role on hormonal profile as well as menstrual regularity in obese women with PCOS more than diet regime and exercise alone.

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Authors' contributions

The authors have determined that all individuals indicated as authors are eligible for authorship. The content and similarity index of the paper are the responsibility of all authors who have critically evaluated and approved the final version.

Availability of data and materials

The collected and analyzed data during the study are available upon reasonable request and following institutional approval from the corresponding author. **Conflict of interest**

This article has no potential for a conflict of interest.

Disclosure statement

No author has a financial stake in or has benefited financially from this study.

Competing interests

The authors state that they do not have any competing interests.

References

1. Alessa A, Aleid D, Almutairi S, AlGhamdi R, Huaidi N, Almansour E. Awareness of polycystic ovarian syndrome among Saudi females. *International Journal of Medical Science and Public Health*. (2017). 6(6): 1013-1020.
2. Teede H, Misso M, Costello M, Dokras A, Laven J, Moran L, & et al. International PCOS Network. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. *Clin Endocrinol (Oxf)*. (2018). 89(3):251-268.
3. Amiri M, Ramezani Tehrani F, Behboudi-Gandevani S, Bidhendi-Yarandi R, & Carmina E. Risk of hypertension in women with polycystic ovary syndrome: a systematic review, meta-analysis and meta-regression. *Reproductive Biology and Endocrinology*. (2020). 18(1): 1-15.
4. De Groot P, Dekkers O, Romijn J, Dieben S, Helmerhorst F. PCOS, coronary heart disease, stroke and the influence of obesity: a systematic review and meta-analysis. *Human reproduction update*. (2011). 17(4): 495-500.
5. Orio F, Muscogiuri G, Nese C, Palomba S, Savastano S, Tafuri D, & et al. Obesity, type 2 diabetes mellitus and cardiovascular disease risk: an update in the management of polycystic ovary syndrome. *Eur J Obstet Gynecol Reprod Biol*. (2016). 2(7): 214-219.
6. Chemerinski A, Cooney L, Shah D, Butts S, Gibson-Helm M, Dokras A. Knowledge of PCOS in physicians-in-training: identifying gaps and educational opportunities. *Gynecol Endocrinol*. (2020). 36(10): 854-859.
7. Bartow M, Raggio B. Liposuction. [Updated Feb 14]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. (2024)
8. Savacini M, Bueno D, Molina A, Lopes A, Silva C, Moreira R, & et al. Effectiveness and safety of contrast cryolipolysis for subcutaneous-fat reduction. *Dermatol Res Pract*. (2018). 2(9): 527-535.
9. Sasaki G, Abelev N, & Tevez-Ortiz A. Noninvasive selective cryolipolysis and reperfusion recovery for localized natural fat reduction and contouring. *Aesthet Surg J*. (2014). 34(3): 420-431.
10. McGee D, & Diverse Populations Collaboration. Body mass index and mortality: a meta-analysis based on person-level data from twenty-six observational studies. *Annals of Epidemiology*. (2005). 15(2): 87-97.
11. Mawaddatina T, Budihastuti U, & Rahayu D. Waist circumference, hip circumference, arm span, and waist-to-hip ratio high risk of polycystic ovarian syndrome. *Scottish Medical Journal*. (2021). 66(4): 186-190.
12. Malini N, & George K. Evaluation of different ranges of LH: FSH ratios in polycystic ovarian syndrome (PCOS)—Clinical based case control study. *Gen Comp Endocrinol*. (2018). 2(6): 51-57.
13. Mehrabian F, Khani B, Kelishadi R, Ghanbari E. The prevalence of polycystic ovary syndrome in Iranian women based on different diagnostic criteria. *Endokrynol Pol*. (2011). 62(3): 238-242.
14. Shetty D, Chandrasekaran B, Singh AW & Oliverraj J. Exercise in polycystic ovarian syndrome: An evidence-based review. *Saudi Journal of Sports Medicine*. (2017). 17(3): 10-17.
15. YShek, S, Chan, N, & Chan, H. Non-invasive cryolipolysis for body contouring

- in Chinese—a first commercial experience. *Lasers in Surgery and Medicine*. (2012). 44(2): 125-130.
16. Louwers Y, & Laven J. Characteristics of polycystic ovary syndrome throughout life. *Ther Adv Reprod Health*. (2020). 2(7): 116-120.
 17. Napoleão A, Fernandes L, Miranda C, Marum A. Effects of Calorie Restriction on Health Span and Insulin Resistance: Classic Calorie Restriction Diet vs. Ketosis-Inducing Diet. *Nutrients*. (2021). 13(4): 45-52.
 18. Slentz C, Houmard J, & Kraus W. Exercise, abdominal obesity, skeletal muscle, and metabolic risk: evidence for a dose response. *Obesity (Silver Spring)*. (2009). 3(3): 27-33.
 19. Hsu K, Liao C, Tsai M, Chen C. Effects of Exercise and Nutritional Intervention on Body Composition, Metabolic Health, and Physical Performance in Adults with Sarcopenic Obesity: A Meta-Analysis. *Nutrients*. (2019). 11(9):21-30.
 20. UKaur I, Suri V, Sachdeva N, Rana SV, Medhi B, Sahni N, & et al. Efficacy of multi-strain probiotic along with dietary and lifestyle modifications on polycystic ovary syndrome: a randomised, double-blind placebo-controlled study. *Eur J Nutr*. (2022). 61(8):41-45
 21. Meyer P, da Silva R, Oliveira G, Tavares M, Medeiros M, Andrada C, & et al. Effects of Cryolipolysis on Abdominal Adiposity. *Case Rep Dermatol Med*. (2017). 38(5):379-386.
 22. Ingargiola M, Motakef S, Chung M, Vasconez H, Sasaki G. Cryolipolysis for fat reduction and body contouring: safety and efficacy of current treatment paradigms. *Plast Reconstr Surg*. (2015). 135(6):1581-1590.
 23. Hwang I, Kim K, & Lee K. Cryolipolysis-induced abdominal fat change: Split-body trials. *PLoS One*. (2020). 15(12): 373-395.
 24. Falster M, Schardong J, Santos D, Machado B, Peres A, Rosa P, et al. (2019).. Effects of cryolipolysis on lower abdomen fat thickness of healthy women and patient satisfaction: a randomized controlled trial. *Braz J Phys Ther*. (2020). 24(5):441-448.
 25. Berryman D, Glad C, List E, Johannsson G. The GH/IGF-1 axis in obesity: pathophysiology and therapeutic considerations. *Nat Rev Endocrinol*. (2013). 9(6):346-356.
 26. Wang F, Dou P, Wei W, Liu P. Effects of high-protein diets on the cardiometabolic factors and reproductive hormones of women with polycystic ovary syndrome: a systematic review and meta-analysis. *Nutr Diabetes*. (2024). 14(1): 38-41.
 27. Brann D, Putnam-Roberts C, Mahesh V. Progesterone and corticosteroid regulation of hypothalamic and pituitary opioid content during LH surge induction. *Mol Cell Neurosci*. (1992). 3(3):191-198.
 28. Cowan S, Lim S, Alycia C, Pirota S, Thomson R, Gibson-Helm M, & et al. Lifestyle management in polycystic ovary syndrome – beyond diet and physical activity. *BMC Endocr Disord*. (2023). 23(1): 86-92.
 29. Abdel-Aal N, Elerian A, Elmakaky A, Alhamaky D. Systemic Effects of Cryolipolysis in Central Obese Women: A Randomized Controlled Trial. *Lasers Surg Med*. (2020).52(10):971-978.
 30. Badran S, Doi S, Iskeirjeh S, Aljasseem G, Jafarian N, Clark J, et al. Metabolic changes after nonsurgical fat removal: A dose response meta-analysis. *J Plast Reconstr Aesthet Surg*. (2023). 7(7) :68-77.
 31. Hutchison S, Stepto N, Harrison C, Moran L, Strauss B, Teede H. Effects of exercise on insulin resistance and body composition in overweight and obese women with and without polycystic ovary syndrome. *J Clin Endocrinol Metab*. (2011). 9(6):48–56.
 32. Stamatiades G, Kaiser U. Gonadotropin regulation by pulsatile GnRH: Signaling and gene expression. *Mol Cell Endocrinol*. (2018). 5(4):131-141.
 33. Beals K, & Hill A. (2006). The prevalence of disordered eating, menstrual dysfunction, and low bone mineral density among US collegiate athletes. *Int J Sport Nutr Exerc Metab*. (2006).16(1):1-23.
 34. Costa A, Oliveira S, Brito A, Lopes L, Primo M, Sales A, & et al. Cryolipolysis on More than One Body Area Increases Lipid Peroxidation without Changing Lipid

Profile and Inflammatory Markers. *Biology*
(Basel). (2022). 11(12):1690-1699.