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The influence of physical activity, diet, and lifestyle of patients on the course of polycystic ovary syndrome (PCOS) in women

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Abstract

Polycystic ovary syndrome (PCOS) is an endocrine disorder caused by multiple genetic and environmental factors, affecting women of reproductive age but extending across all stages of a woman's life [1]. Major symptoms in many PCOS patients include menstrual cycle irregularities, difficulties in maintaining normal body weight, excessive body hair growth, acne, and fertility problems. The prevalence of PCOS varies depending on the definition used, ranging between 6-20%, making it the most common endocrine disorder among women of reproductive age [2,3]. It accounts for approximately 80% of cases of anovulatory infertility, disrupting various stages of the reproductive axis. Evidence from numerous studies suggests that lifestyle modification should be the first-line therapy for women with PCOS [4]. This paper focuses on research evaluating the treatment of this condition through lifestyle changes, physical activity, and diet. Such therapeutic interventions can significantly improve clinical outcomes and the health profile of PCOS patients by promoting favorable changes in body composition, partially normalizing sex hormone levels, reducing inflammatory parameters, and improving mental health. Therefore, the adoption of comprehensive lifestyle modifications is crucial in the treatment of polycystic ovary syndrome.

Key words: PCOS, polycystic ovary syndrome, physical activity, diet, lifestyle

Introduction

Polycystic ovary syndrome (PCOS) is an endocrine disorder caused by multiple genetic and environmental factors, affecting women of reproductive age but extending across all stages of a woman's life [1]. Major symptoms in many PCOS patients include menstrual cycle irregularities, difficulties in maintaining normal body weight, excessive body hair growth, acne, and fertility problems. The prevalence of PCOS varies depending on the definition used, ranging between 6-20%, making it the most common endocrine disorder among women of reproductive age [2,3]. It also accounts for approximately 80% of cases of anovulatory infertility, disrupting various stages of the reproductive axis. Evidence from numerous studies suggests that lifestyle modification should be the first-line therapy for women with PCOS [4]. This paper aims to focus on studies assessing the treatment of this condition through lifestyle changes, physical activity, and diet.

Diagnostic Criteria

Diagnostic criteria for women of reproductive age, adopted by ESHRE/American Society for Reproductive Medicine (ASRM) in Rotterdam in 2004, include the presence of two out of three of the following clinical symptoms: ovulation disorders (oligo-ovulation or absence of ovulation), clinical and/or biochemical signs of hyperandrogenism, and polycystic ovarian morphology (PCOM) on ultrasound examination [5]. For adolescents, the diagnosis of PCOS requires the presence and persistence of at least two years after menarche: irregular menstrual cycles, particularly rare cycles (oligomenorrhea), secondary and primary amenorrhea, and biochemical hyperandrogenism or clinical hyperandrogenism (progressive hirsutism) [6].

Clinical Picture

Symptoms observed in patients with PCOS include irregular menstrual cycles, difficulty conceiving, increased tendency toward weight gain, difficulty losing weight, excessive body hair growth, hair loss on the scalp, acne, and often mood disorders characterized by low mood. Additionally, these symptoms may be accompanied by coexisting diseases and disorders such as insulin resistance, type 2 diabetes, gestational diabetes,

cardiovascular diseases, fatty liver, obstructive sleep apnea, mood disorders, anxiety, depression, and even endometrial cancer [7].

Pathophysiology and Hormonal Disorders

Several hypotheses attempt to explain the pathophysiology of PCOS. PCOS is known as a multifactorial disease where genetic and environmental factors lead to uncontrolled ovarian steroidogenesis, aberrant insulin signaling, and excessive oxidative stress. The internal defect of the thecal cells in PCOS is known to cause hyperandrogenemia by influencing granulosa cells and overproducing anti-Müllerian hormone (AMH). It has also been studied that insulin resistance and hyperandrogenism in these patients may result from mitochondrial dysfunction leading to increased glycolytic-oxidative stress [8]. As a result of various known and unknown mechanisms, women with PCOS experience abnormal gonadotropin secretion. This leads to increased LH secretion and an increased LH/FSH ratio >2.5 . LH can be responsible for the growth of ovarian thecal cells, creating an anatomopathological substrate conducive to hyperandrogenism. The FSH level remains low or normal but constant, stimulating the growth of new follicles which, instead of ovulating, undergo atresia. These follicles join the stromal part of the ovary, which under the influence of LH secretes a steady amount of androgens. There are reports that LH and FSH secretion disorders may result from altered hypothalamic secretion of GnRH or increased pituitary sensitivity to this hormone. GnRH may stimulate excessive LH synthesis. It has also been shown that excess androgens in ovarian follicles lead to increased inhibin activity, which can partially inhibit FSH, increase FSH sensitivity to negative estrogen feedback, and relative insensitivity to GnRH. Women with PCOS have elevated levels of circulating estrone (E1) and estradiol (E2) due to increased peripheral aromatization of androgens to estrone and androgen-dependent aromatase activity in ovarian granulosa cells. This chronic state of hyperestrogenism may promote endometrial proliferation and increase the risk of hyperplasia and even endometrial cancer. Estrogen levels in these women reach those present in the early follicular phase of healthy women, resulting in anovulation. Chronic anovulation is associated with decreased progesterone secretion. In PCOS, ovarian-origin hyperandrogenism is mainly due to defective internal steroidogenesis in thecal cells, resulting from increased activity of enzymes catalyzing several stages of androgen synthesis, as well as the production of AMH and inhibin by granulosa cells. Additionally, PCOS involves adrenal-origin hyperandrogenism and increased peripheral cortisol metabolism. Furthermore, PCOS is associated with

decreased levels of sex hormone binding globulin (SHBG), which is responsible for binding sex hormones, and increased levels of AMH [8].

It is worth noting that hyperandrogenism in PCOS promotes insulin resistance and hyperinsulinemia, which in turn exacerbate hyperandrogenemia and can lead to weight gain and obesity. Conversely, overweight, obesity, along with insulin resistance and hyperinsulinemia, may further stimulate steroidogenesis and androgen production, exacerbating disease symptoms [9].

White adipose tissue is an active endocrine organ. Adipocytes and macrophages secrete adipokines, hormones that have a significant impact on the body [10].

Altered levels of several adipokines have been noted in women with PCOS. They have reduced levels of adiponectin, which is responsible, among other things, for insulin sensitivity, and increased levels of visfatin and resistin, leading to insulin resistance and increased systemic inflammation [9]. Leptin, another adipokine, plays a role in regulating long-term food intake and energy expenditure and can lead to increased cardiometabolic risk. Researchers have found increased levels of leptin and leptin resistance in individuals with PCOS (both obese and lean) [11].

Physical Activity

Among the many medical recommendations proposed for women with PCOS, doctors commonly recommend engaging in physical activity. However, this paper seeks to answer the specific question of what types of physical exercises should be recommended to patients with this condition to achieve optimal treatment results. We will start by analyzing how physical exercises can modify laboratory test results and the clinical picture of PCOS in women.

Body Weight and BMI

Many women with PCOS struggle with obesity or overweight. Studies have shown that physical exercise alone may have a limited impact on BMI (body mass index) in women with PCOS, but it can reduce waist circumference and improve other indicators of body composition, including increased lean mass and reduced fat mass. These changes can occur without a change in total body weight. However, according to widespread knowledge, sufficiently intense physical activity leads to weight loss and reduced body fat content, which certainly has a beneficial effect on the health of PCOS patients [12].

In one meta-analysis [12] examining the impact of physical exercise on the health of women with PCOS, improvements were found in cardiorespiratory fitness (VO₂peak), BMI, WC (waist circumference), and various metabolic health markers, including fasting insulin and HOMA-IR (homeostatic model assessment for insulin resistance), particularly compared to a control group without exercise. The greatest improvements in health parameters were demonstrated by intense exercises of high intensity, both alone and in combination with dietary interventions. Moderate-intensity exercises resulted in significant improvements in VO₂peak, WC, and BMI in combination with diet. Resistance training improved FAI (free androgen index) and HOMA-IR compared to the control group.

Aerobic exercises

Aerobic exercises of varying intensities result in the improvement of peak VO₂. Peak VO₂ is a measure of cardiorespiratory fitness and an important indicator of health and mortality in women with PCOS. Research findings suggest that at least 120 minutes of intense physical activity per week are needed to achieve beneficial health outcomes in women with PCOS [13].

Randomized controlled trials (RCTs) have been conducted on women with PCOS using aerobic exercises, including treadmill exercises or cycling under the supervision of medical, sports, or research personnel. The duration of the studies was three months, during which participants cycled for 30 minutes, three days a week at 60–70% of VO₂ max. This physical effort led to a decrease in fasting insulin levels (FI) but without significant changes in sex hormones such as LH or sex hormone-binding globulin (SHBG) [14, 15].

In another 24-week study with similar cycling parameters, comparable results were achieved. However, improved fasting insulin levels did not persist in a 12-week program followed by a 12-week training break [15]. Cycling for 12 weeks, 60 minutes five days a week at 65% of VO₂ max, improved insulin sensitivity (IS) and glucose infusion rate (GIR) during hyperinsulinemic-euglycemic clamp, and also led to a reduction in insulin C peptide [16].

However, another study conducted over 16 weeks, involving continuous aerobic training (CAT) or intermittent aerobic training (IAT) on a treadmill, observed a decrease in total testosterone (TT) in both exercise groups and a lower free androgen index (FAI) in the IAT group.

In a study that included a 16-week intervention involving walking and a follow-up visit after 32 weeks from the start of the study, decreases in free testosterone (fT) and DHEA-

S were observed at both 16 and 32 weeks, with reductions in estrone sulfate and estradiol (E2) after 16 weeks [17].

In a six-month study where patients engaged in brisk walking for 20–60 minutes at least three days a week, insulin and FAI levels, as well as thyroxine, remained unchanged [18]. A more structured 16-week individual aerobic treadmill training program at 55% of VO₂ max for five days a week improved glucose disposal rate and atrial natriuretic peptide measure, although TT, FAI, FI, and atrial natriuretic peptide did not change significantly [19].

Training programs focusing on aerobic exercises, particularly those involving more intense activity and/or more frequent weekly exercises or longer sessions, can improve insulin measurements and insulin response. Aerobic exercises have little impact on changes in sex hormones, SHBG, and LH. A small number of studies conducted so far in women with PCOS have not shown any changes in adiponectin following aerobic exercise interventions.

A pilot study examined the effects of high-intensity interval training and strength training on metabolic, cardiovascular, and hormonal outcomes in women with polycystic ovary syndrome (PCOS) [20]. Thirty-one women with PCOS (mean age 27.2 ± 5.5 years; BMI 26.7 ± 6.0 kg/m²) were randomly assigned to high-intensity interval training, strength training, or a control group. The exercise groups exercised three times a week for 10 weeks. The main assessment parameter was the change in homeostatic model assessment of insulin resistance (HOMA-IR), which significantly improved only after high-intensity interval training. Following high-intensity interval training, high-density lipoprotein cholesterol increased by 0.2 mmol/l, and endothelial function, measured as flow-dependent dilation of the brachial artery, increased by 2.0%. Body fat percentage decreased significantly after both exercise regimens, without changes in body weight. Following strength training, anti-Müllerian hormone levels were significantly reduced by -14.8 pmol/l. A 10-week high-intensity interval training improved insulin resistance in women with PCOS without weight loss. Moreover, body composition significantly improved after both strength and high-intensity interval training. This study demonstrates that exercise training can improve the cardiometabolic profile in women with polycystic ovary syndrome [21].

In light of the many studies mentioned above [9], it is valuable to summarize the findings regarding physical exercise in PCOS. First, when treating a patient with PCOS, it is important to inquire about and emphasize the role of physical activity in her life and then provide appropriate recommendations. To achieve favorable insulin-related effects, vigorous aerobic activity should be performed at least three days a week for 30 minutes or more, controlled by VO₂max intensity ($\geq 60\%$ VO₂max). In addition, strength training (ST) and

progressive resistance training (PRT) performed on non-consecutive days three times a week may provide additional benefits in terms of androgen levels. It is also worthwhile to include yoga in regular physical exercise routines, which, although poorly studied, may offer benefits in terms of androgens and insulin sensitivity.

Further research is necessary to determine which types and amounts of physical activity can lower androgen levels or increase SHBG levels. These studies should focus on the regularity of menstrual cycles and ovulation, as well as LH and FSH, as a decrease in these hormones may indicate more regular ovulation and/or appropriate follicular maturation. More research is still needed to determine the impact of different exercise forms on adipokines and AMH in women with PCOS.

Exercise and inflammation in PCOS

Research underscores that PCOS is often associated with chronic inflammation [22]. During a meta-analysis of studies examining the effects of exercise on inflammatory markers in PCOS, researchers demonstrated that physical training effectively reduces CRP levels in serum compared to control groups [23]. In one study [24] comparing the effects of aerobic and resistance exercises in middle-aged patients with hypertension, the results showed that while both types of training may be effective in reducing blood pressure and improving endothelial function, only aerobic training reduced inflammatory markers such as CRP, vascular cell adhesion molecule-1, and oxidized LDL-like lectin-1 receptor. However, resistance exercises may simultaneously play a positive role in reducing inflammatory markers such as NF- κ B, IFN- γ , and eotaxin-1 after 12 weeks of intervention. However, the study population consisted of obese elderly women, which could be corrected in future studies [25].

Mental health and physical activity

It is worth noting that aside from cardiometabolic and reproductive complications, PCOS is associated with an increased prevalence of mental health disorders such as anxiety disorders, body image dissatisfaction, and depression. Studies show that physical activity improves mental well-being in women with PCOS, depending on certain physiological factors. Therefore, in addition to tangible evidence of physical health improvements in patients with PCOS, physical activity also enhances their mental condition. Establishing a universal amount of exercise required to achieve the desired result is difficult as it is always an individual matter. However, guidelines for PCOS suggest at least 150 minutes of physical activity per

week. Evidence confirms that this should form the basis of medical recommendations for women with PCOS [26].

Diet

Polycystic ovary syndrome (PCOS) is caused by abnormal androgen production. This condition worsens the quality of life for women, disrupting their physiology and psychology during their reproductive years. PCOS may also be associated with other diseases such as diabetes and hypertension. Numerous factors, such as an inappropriate lifestyle, unhealthy diet, inadequate care and medication, as well as late diagnosis, contribute to the prevalence of this disease in women. Therefore, early diagnosis and improved management of diet and lifestyle are essential to enhance quality of life and recovery for patients with this disease.

Diet is an important modifying factor in the course of PCOS. Increased adipose tissue is often present in individuals with PCOS. Abdominal obesity in PCOS is associated with increased insulin resistance, which exacerbates metabolic and reproductive abnormalities. Furthermore, androgens promote the accumulation of visceral adipose tissue and insulin resistance by inhibiting lipolysis and promoting lipogenesis. Obesity significantly influences the PCOS phenotype, as it is associated with a higher prevalence of irregular menstrual cycles, hyperandrogenism, and hirsutism [27].

Most studies on excess adipose tissue in PCOS have relied on approximate indicators of total mass, such as body mass index (BMI). In practice and scientific research, the PCOS obesity phenotype differs from the leanness phenotype based on BMI, meaning it is found above or below the normal limit for age and ethnic origin [28].

More helpful and accurate body composition indicators include imaging methods such as computer tomography (CT), magnetic resonance imaging (MRI), and dual-energy X-ray absorptiometry (DEXA) [29]. These methods allow for more accurate imaging of fat distribution and adipose tissue function.

Both obese and non-obese women with PCOS are metabolically worse off compared to their age- and BMI-matched control groups and have more visceral adipose tissue. Non-obese women with PCOS pose similar risks to those with obesity, having a similar visceral adipose tissue volume (adjusted for body mass). Non-obese PCOS is associated with similar risks to those of obese PCOS, because it has a similar amount of visceral fat [29].

Weight loss is typically considered first-line treatment for women exhibiting the obesity phenotype, which is not necessary for weight loss in thin women. Instead, for thin women with PCOS, the main goal is weight maintenance. Many lifestyle modifications, such as

dietary interventions and regular physical activity, have shown improvement in insulin resistance and alleviation of hyperandrogenism, among other beneficial effects on PCOS symptoms [30].

The Mediterranean diet (MD) is an internationally recognized dietary model associated with beneficial dietary patterns. Adherence to MD involves consuming foods rich in fiber and plant proteins. MD is a well-established, health-promoting dietary pattern. In particular, there is evidence that adherence to MD is inversely correlated with obesity, insulin resistance (IR), and the risk of type 2 diabetes and cardiovascular diseases. Based on this, MD may be considered one of the best dietary strategies for treating women with PCOS.

In particular, a seven-day dietary record analysis showed that women with PCOS had a different dietary pattern, with higher consumption of simple carbohydrates and SFA and lower consumption of complex carbohydrates, fiber, and monounsaturated fatty acids compared to the control group. Interestingly, this unhealthy dietary pattern was associated with more severe hyperandrogenism, inflammation, and IR. Specifically, inflammation, adherence to MD, and consumption of monounsaturated fatty acids were factors that had the strongest impact on testosterone levels [31].

To date, very low-calorie ketogenic diets have been considered effective dietary interventions for short-term PCOS treatment. It promotes rapid weight loss, improves body composition and metabolic profile (waist circumference, fat mass, blood glucose level, HbA1c and HOMA-IR), and enhances insulin sensitivity, fundamental aspects of PCOS pathophysiology. Given its complexity, this dietary intervention must be recommended and managed by qualified specialists in this field. Additionally, it is essential to individualize treatment and assess contraindications and side effects. This type of diet is proposed in stages, with the first being the most restrictive. It is important to adhere to each stage of the diet properly to achieve long-term weight loss and maintain a healthy lifestyle [32].

Conclusion

Polycystic ovary syndrome is a disease that affects the entire body of a woman. Therefore, it is important for doctors from many specialties to consider the health consequences of this disease and be able to help these patients. It is important to remember the basic therapeutic interventions for PCOS, such as diet and physical activity. Based on the above information, we see that the role of exercise training in the treatment of PCOS cannot be underestimated, as it improves the fitness of patients, leads to weight loss, improves body composition and cardiometabolic, and even hormonal outcomes.

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Author's contribution

Conceptualization, GRS, DR, PSR, WK; methodology, GRS, BJ, JD; software, WK, RO; check, GRS, MB, PSR and DR; formal analysis, DR, GJ; investigation, PRS; resources, WK; data curation RO, MB, PS; writing - rough preparation, PSR, BJ, JD; writing - review and editing, GRS, PS, GJ, JD; visualization, GRS; supervision, PS, BJ, MB; project administration, PSR, GJ, RO; receiving funding, no specific funding.

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