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Review of available treatment methods for polycystic ovary syndrome (PCOS) with special emphasis on diet and physical activity

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ABSTRACT:

Polycystic ovary syndrome (PCOS) occurs in 5 to 10% of women of reproductive age and is the most common cause of anovulation in infertile women.

PCOS is associated with insulin resistance, type 2 diabetes mellitus, and increased cardiovascular risk. Although insulin resistance is not included as a criterion for diagnosis, it is a critical pathological condition of PCOS.

While PCOS can pose challenges to women's health, with appropriate medical care and lifestyle modifications, symptoms can be effectively managed and the risk of associated health complications reduced. Behavioral, medical and surgical treatments have been evaluated in order to improve the fertility of women with PCOS. Lifestyle modifications (stop smoking, physical exercise and weight loss when necessary) are of the utmost importance.

The aim of this paper is to present the available methods of treatment, prevention of consequences and fertility problems affecting women with PCOS.

Keywords: PCOS, lifestyle, exercise therapy, behavior therapy, diet therapy, reproductive health, metabolic health, physical activity, metformin, inositols, oral contraceptives, clomiphene citrate

Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age. It is characterized by various symptoms and can impact reproductive, metabolic, and emotional health in women.

PCOS is diagnosed via the internationally endorsed Rotterdam criteria, which require the presence of two or more features including [1]

1. Ovarian dysfunction: Typically involving hormonal disturbances leading to irregular or absent menstrual periods, infrequent ovulation, and increased production of male hormones (androgens).
2. Hyperandrogenism: Elevated levels of androgens (e.g., testosterone) in the body, which can result in symptoms such as acne, excessive hair growth (hirsutism), and weight issues.
3. Presence of multiple ovarian cysts: Visible on ultrasound, multiple small cysts on the ovaries that may not ovulate.

In addition, PCOS may be associated with other metabolic disorders such as insulin resistance (which can lead to carbohydrate metabolism disturbances and type 2 diabetes), lipid disorders (elevated cholesterol and triglyceride levels), and increased risk of cardiovascular diseases.[2]

PCOS presents in different forms and severity of symptoms, so diagnosis is based on a combination of clinical symptoms, hormonal tests, and ovarian ultrasound findings. Treatment typically involves pharmacological therapy, lifestyle changes (including diet and regular physical activity), and may require psychological support[3].

Exercises

The meta-analysis from 2020 demonstrated that physical training in women with polycystic ovary syndrome (PCOS) improves metabolic and cardiovascular outcomes, both in the presence and independently of anthropometric changes, supporting the role of exercise therapy as a first-line approach to improving health outcomes in women with PCOS. The studies conducted showed a positive impact on the health of women with PCOS from both aerobic and strength training [1].

Achieving an ideal relationship between exercise and its effects on PCOS may be challenging due to the unique characteristics of the condition varying greatly among individuals. Recommendations for PCOS typically advise engaging in at least 150 minutes of physical activity per week [4].

Analysis of pooled data indicated statistical favourable effects of exercise on total cholesterol, fasting glucose, waist circumference and waist-to-hip ratio, systolic blood pressure, C-reactive protein, total testosterone, and sex hormone binding globulin [5].

Greenwood et al. conducted a pioneering cross-sectional study to explore the impact of exercise of different intensities on women with PCOS. Their findings revealed that high-intensity interval training (HIT) provides superior health benefits compared to moderate exercise for women with PCOS, independent of age, BMI, and total exercise volume. Specifically, engaging in 60 minutes of vigorous activity per week was associated with a significant 22% reduction in the odds ratio of developing metabolic syndrome among this population. [6] [7].

Diet

While reducing calorie intake and promoting weight loss is recommended for obese women with PCOS, most dietary recommendations are based on studies of obese women without PCOS. Evidence is limited regarding the superiority of any specific diet. Some studies indicate that a low-carbohydrate diet (less than 45% of total daily calories) can help reduce body mass index and total cholesterol levels in PCOS patients.

Additionally, a high-protein diet has been shown to promote weight loss compared to a standard protein diet. However, no significant differences were found between a vegan diet and a calorie-restricted diet, or between a low-glycemic-index diet and a hypocaloric healthy eating diet. [8] [9].

It has been recommended that a balanced diet with 40% energy from carbohydrates, 30% from fats, and 30% from protein with optimum physical activity could reduce severe PCOS symptoms and improve metabolic balance [10].

The very low-calorie ketogenic diet (VLCKD) is increasingly showing promise for not only obesity but also other metabolic diseases. Current data suggest that VLCKD can be an effective short-term treatment for PCOS, promoting rapid weight loss and improving body composition and metabolic profiles, including waist circumference, fat mass, blood glucose, HbA1c, and HOMA-IR. It also enhances insulin sensitivity, which is crucial in the pathophysiology of PCOS. Due to its complexity, this diet should be recommended and supervised by qualified professionals [11]

Researchers investigated how vitamin D supplementation affects the health of patients with PCOS. Findings from existing randomized controlled trials suggest that vitamin D supplementation could improve LH levels and help regulate the menstrual cycle in PCOS patients, but it does not impact FSH levels or the LH/FSH ratio [12].

Pharmacological therapy – metformin therapy

One of the most important medications used in the treatment of women with PCOS is metformin, which exhibits hypoglycemic effects. Metformin appears to be an effective intervention for overweight women with PCOS [13].

It has been proven that in women with PCOS, metformin reduces hyperinsulinemia, decreases LH and testosterone levels. It also positively affects lipid metabolism by lowering cholesterol and triglyceride levels in the blood and contributes to weight loss. Additionally, it may positively influence the regularity of menstrual cycles and ovulation in women with PCOS [13].

Metformin alone increases the ovulation rate in women with polycystic ovary syndrome (PCOS) compared to a placebo, but it should not be the first-line treatment for anovulation. Oral ovulation induction agents like clomiphene citrate or letrozole are more effective at increasing ovulation, pregnancy, and live-birth rates in women with PCOS. There is moderate evidence that discontinuing metformin at the onset of pregnancy does not increase miscarriage rates, but there is insufficient evidence that combining metformin with other ovulation-inducing agents increases live-birth rates [14].

Pharmacological therapy – OCP (oral contraceptive pill)

OCPs are one of the most common methods of treating PCOS chosen by gynecologists. However, it should be noted that these medications do not treat the cause of PCOS; they work symptomatically to alleviate symptoms. After discontinuing their use, the symptoms will likely return to their pre-treatment state.

The use of OCPs is generally considered the first-line treatment. The aim is to regulate menstrual cycles and reduce hyperandrogenemia.

Recommended OCPs include those with 20-35 mcg of ethinylestradiol and progestin, particularly those with antiandrogenic properties like drospirenone or norgestimate. Combination therapy through a transdermal patch or vaginal ring is also an option. Although they have a low incidence of general side effects, progestin-only contraception is not ideal for these patients. Without estrogen, progestin-only options do not increase SHBG levels, leading to a lesser reduction in the free androgen index [15][16].

While OCPs are effective in managing PCOS symptoms, they may come with side effects, including: nausea, weight gain, mood changes, breast tenderness, increased risk of blood clots. Long-term OCPs use has been linked to an increased risk of venous thromboembolism, hypertension, dyslipidemia, low-density lipoprotein (LDL) elevation, dysglycemia, and cancer in women [17].

Pharmacological therapy – Inositols

Myoinositol (MI) and D-chiro-inositol (DCI) play critical roles in various biochemical pathways within oocytes, influencing processes such as oocyte maturation, fertilization, implantation, and post-implantation development. These inositols are also involved in insulin signaling and hormone synthesis specifically within the ovaries. Their presence and balance are essential for supporting these physiological processes effectively. It belongs to the vitamin B complex and has been shown to improve various metabolic and reproductive aspects of PCOS [18].

Numerous studies have shown that administering myoinositol to patients with polycystic ovarian syndrome (PCOS) enhances ovarian function and fertility. It reduces the severity of hyperandrogenism symptoms such as acne and hirsutism, positively impacts metabolic factors, and regulates hormonal parameters crucial for reproductive health and ovulation. Consequently, myoinositol treatment has emerged as a novel approach to alleviate PCOS symptoms, promote spontaneous ovulation, and facilitate induced ovulation [18].
A study was conducted comparing the effect of metformin combined with myoinositol (group I) versus metformin alone (group II) on the health and fertility of women with PCOS.

Group I, which received the combination of metformin and myoinositol, showed marked improvement in menstrual cycles, including cycle length and number of bleeding days, compared to Group II, which received metformin alone. Both groups demonstrated comparable improvements in biochemical and hormonal parameters after three months. Importantly, the live birth rate was significantly higher in Group I (55%) compared to Group II (26.67%). The study concluded that the combination of metformin and myoinositol led to a significantly higher live birth rate compared to metformin alone in women with PCOS [19].

Pharmacological therapy - Clomiphene citrate

Clomiphene citrate is a medication commonly used to treat infertility in women, particularly those with polycystic ovary syndrome (PCOS). It works by stimulating ovulation. Clomiphene citrate is an oral selective estrogen receptor modulator (SERM) that induces the pituitary gland to release hormones necessary for ovulation to occur [20].

After using the medication, ovulation is achieved in 56-73% of infertile patients. The remaining women show varying degrees of resistance to it. Clomiphene does not affect insulin resistance, which is an important component of PCOS [20].

Clomiphene citrate remains the first line of medical treatment of infertility in women with PCOS in absence of other male or female causes of infertility [21].

Conclusions

The prevalence of PCOS is notably high among women of reproductive age, with significant consequences warranting the exploration of nutritional interventions.

Although PCOS is often linked to obesity, it also affects women of normal weight. For those who are overweight or obese, interventions focus on weight reduction and maintaining a healthy weight.

Pharmacological methods exist to support women with PCOS, but none can completely cure the condition or prevent its consequences. Therefore, the significance of dietary and physical activity approaches has become evident. While drug therapy can be effective in the short term, a personalized diet combined with an exercise routine is likely the only sustainable solution.

Disclosure:

Authors' contribution:

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