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Current Status of Research on Improving Polycystic Ovary Syndrome Through Dietary Interventions and Exercise

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Abstract: Polycystic Ovary Syndrome (PCOS) is a common gynecologic disorder that affects women of childbearing age, and the disorder primarily affects metabolic and reproductive health. Research on the pathogenesis of PCOS is now more complete, and there is a wide variety of tools for the management of PCOS, each with its own advantages. However, patients with PCOS still have some difficulty in finding interventions that are appropriate for their situation. This paper combines the pathogenesis of PCOS, further analyzes several representative dietary interventions and exercise interventions, and finds that in improving insulin resistance and reproductive health, PCOS patients should adopt interventions that are compatible with their own backgrounds and living conditions before further effective PCOS management is possible. This paper provides a reference for future research on dietary and exercise interventions, while the data supporting the effectiveness of the post-intervention effects on PCOS remain lacking, and future research could focus on the effectiveness of interventions in PCOS patients under different pathogenic mechanisms, in order to formulate more reasonable management strategies.

Keywords: Polycystic Ovary Syndrome, Etiology, Dietary Interventions, Exercise Interventions, PCOS Management

1. Introduction

Polycystic ovary syndrome (PCOS) is a common gynecologic endocrine disorder that affects the reproductive health and metabolic function of 11-13% of women worldwide [1]. Patients with PCOS often present with irregular menstruation, hyperandrogenemia, etc. The disorder has also been associated with an increased risk of cardiovascular disease and type 2 diabetes. At the same time, the pathogenesis of PCOS is also very complex, there is no exact direct cause by one factor, but presents a variety of internal and external factors, at the same time, these factors have a certain degree of correlation, the internal causes are mostly inflammation and insulin resistance, etc., and the external causes are genetics and environmental toxins, etc., which according to the study shows that most of the patients with PCOS suffer from insulin resistance, and it plays a key role in the pathogenesis of PCOS [2]. In addition, existing lifestyle interventions can improve the metabolic health of PCOS patients, which include diet, exercise, psychological state and sleep. One study found effective responses and no significant differences between PCOS and non-PCOS patients through lifestyle interventions, suggesting that lifestyle interventions can be an important part of PCOS management [3].

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In today's world, dietary and exercise interventions are known to be effective and varied means of lifestyle interventions that can be used and managed in patients with PCOS. On the one hand, dietary interventions control the intake of blood glucose, carbohydrates, and other nutrients, while on the other hand, exercise interventions improve insulin resistance, reduce androgen levels and improve cardiovascular health, both of which have a significant impact on the management of PCOS. In this study, the diagnostic criteria of PCOS will be selected to analyze the pathogenesis in terms of insulin resistance, inflammation, obesity, hyperandrogenemia, and epigenetic factors, and discuss the correlations and impressions. Secondly, in terms of dietary interventions, this paper will demonstrate the effects of various dietary patterns such as low glycemic index diet and pulse-based diet (PBD), on the management of PCOS, and the section of the paper will also elaborate on the management of supplements and compare them, and it will also organize and summarize aerobic and resistance exercise in order to elaborate on the effects of different intensity, frequency, and duration of exercise on PCOS. Finally, the current status and trend of the development of dietary and exercise interventions for PCOS are summarized, and positive recommendations are made based on the results of the objective analysis to provide a more direct basis for the subsequent management of PCOS.

2. Pathogenesis

The pathogenesis of PCOS is not yet fully understood, but there is a strong relationship with insulin resistance and gut flora, as well as interactions with obesity, inflammation and hyperandrogenemia, and external genetic factors that further enhance the complexity of the disease. This has led to an ongoing controversy over its diagnosis, and after a series of diagnostic criteria have been extrapolated, the Rotterdam Criteria are currently the most widely accepted diagnostic approach to PCOS, but they do not completely correctly diagnose the disease. Therefore, care should also be taken when diagnosing PCOS knowing the various current pathogenic factors, combining the diagnostic criteria and objective circumstances, and excluding other diseases that may cause similar symptoms, and ensuring that patients receive a timely and appropriate diagnosis.

2.1. Diagnostic criteria

The diagnostic criteria for PCOS have undergone many changes since they were first described by Stein and Leventhal in 1935. In 1990, the National Institutes of Health (NIH) proposed the first clinical definition of PCOS, defining it as a woman with clinical and/or biochemical hyperandrogenemia and oligo-ovulation or chronic anovulation.

In 2003, the Rotterdam criteria expanded the diagnostic criteria for PCOS to any two of the three main features: oligo- or anovulation, hyperandrogenemia, and polycystic ovarian morphology, and the detailed diagnostic criteria and methodology are shown in Table 1, which is based on the modified 2003 Rotterdam criteria [4].

Table 1: Main diagnostic features and methods of PCOS

Feature	Recommended Diagnosis	Assessment Methodology
Oligo-ovulation or anovulation	Prolonged menstrual cycle (>35 days) or less than 8 menstrual cycles per year	Detection of serum progesterone or luteinising hormone (LH)
hyperandrogenism	Clinical manifestations (e.g. hirsutism, acne) or biochemical tests (e.g. elevated serum testosterone levels)	1. Liquid chromatography-mass spectrometry (LC-MS) or extraction/chromatographic immunoassays 2. Calculation of free testosterone index (FTI) or bioavailable testosterone (BioT)
Polycystic ovary pattern	≥20 follicles in one or both ovaries or ovarian volume ≥10 cm^3 by ultrasound examination	Use of transvaginal ultrasound at ≥8MHz

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The clinical manifestations of hyperandrogenemia include hirsutism, acne and elevated serum testosterone levels. High-quality assays such as LC-MS are recommended for its evaluation, but they are costly and infrequently used, and direct assays (e.g., RIA, ELISA, CLIA) are not sufficiently sensitive for the detection of testosterone levels in women [2]. Oligovulation is mainly characterized by prolonged menstrual cycles (>35 days) or fewer than 8 menstrual periods per year, and ovulation can be assessed by serum progesterone or luteinizing hormone if PCOS is suspected but not present as a symptom. Polycystic ovarian morphology is detected by ultrasound with ⩾20 follicles in one or both ovaries or an ovarian volume of ⩾10 cm^3, and requires the use of transducer-guided ultrasound at a frequency of ⩾8 MHz as a means of accurately assessing follicle number and ovarian volume [4].

With this criterion, some other factors still need to be considered. Other conditions that may cause similar symptoms, such as congenital adrenal hyperplasia, thyroid disorders and hyperprolactinemia, should be ruled out prior to diagnosis. In making the diagnosis, the doctor also takes into account the patient's medical history, blood hormone levels and ultrasound findings. The use of the criteria has also been controversial, as it has been debated whether women without hyperandrogenemia, but with oligo-ovulation and polycystic ovarian patterns, should be diagnosed with PCOS. After 22 years of use, the diagnostic criteria should probably be updated.

2.2. Insulin resistance

Insulin resistance is central to the pathogenesis of PCOS, and its mechanisms have not been fully defined. However, it has been suggested that insulin resistance may be associated with impaired autophosphorylation of the insulin receptor. Meanwhile, insulin resistance leads to elevated insulin levels, and this compensatory hyperinsulinemia stimulates non-insulin-sensitive tissues, such as ovarian membrane cells, leading to overproduction of androgens in the ovaries and further development of hyperandrogenemia. In addition, insulin affects ovarian function through a number of pathways, including directly as a co-gonadotropin enhancing LH and indirectly by affecting the regulation of the hypothalamic-pituitary-ovarian axis [2].

The results of one study showed that the prevalence of metabolic syndrome among 100 women with PCOS was 31%, 87% were associated with obesity, and 69% of women with PCOS had insulin resistance, thus it can be found that PCOS itself has a high correlation with insulin resistance and high prevalence of metabolic syndrome [5]. Whereas this resistance generally occurs mainly in the post insulin receptor signaling pathway, factors such as hyperandrogenemia, increased androgen receptor sensitivity and decreased serum lipocalin levels may exacerbate insulin resistance in PCOS [6]. There is a degree of intrinsic association between PCOS and insulin resistance in the clinical diagnosis of PCOS, and therefore women with PCOS should also be screened for this [7].

2.3. Obesity

The link between obesity and PCOS is relatively strong, with 38%-88% of PCOS patients being overweight or obese, which may influence the development of PCOS through insulin resistance (IR) and compensated hyperinsulinemia. Significant weight gain exacerbates insulin resistance in patients with PCOS, which may be mediated through inflammatory pathways, and also contributes to metabolic syndromes such as type 2 diabetes, dyslipidemia, and hypertension. In addition, obesity and PCOS are bi-directional; not only does obesity exacerbate the symptoms of PCOS, but also patients with PCOS are susceptible to developing obesity, turning it into a vicious cycle. In general, because insulin resistance is a key factor in the pathogenesis of PCOS, and weight gain exacerbates this resistance, it seems that obesity cannot be ignored as a consideration in the subsequent treatment and management of PCOS patients [6].

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2.4. Inflammation

PCOS is associated with chronic low-grade inflammation, and studies have shown that the development of chronic inflammation is associated with elevated levels of inflammatory markers, including elevated levels of white blood cell counts (WBCs) in patients with PCOS, as well as significantly higher levels of C-reactive protein (CRP), interleukin 6 (IL-6), and a positive correlation with insulin resistance, body weight and fat mass. Pro-inflammatory cytokines and chemokines (IL-8, MCP-1 and MIP-1α) were elevated in patients with PCOS and were associated with insulin resistance, metabolic syndrome and atherosclerosis. In addition, AGEs (advanced glycosylation end products), which are highly reactive derivatives of proteins or lipids, show elevated levels in patients with PCOS, and at the same time with oxidative stress can form a vicious circle, further exacerbating oxidative stress, which is stimulating in PCOS, and may affect steroidogenesis and follicular development by influencing a variety of enzyme activities [8].

Insulin resistance, a key factor, is also associated with inflammation, and hyperglycemia may exacerbate metabolic and endocrine abnormalities by stimulating the production of tumor necrosis factor (TNF-α) by monocytes, while the proportion of pro-inflammatory M1-type macrophages is increased in obese individuals, leading to systemic low-grade chronic inflammation [2]. In addition, normal-weight women with PCOS also experience impaired insulin signaling due to inflammatory processes in adipose tissue. Secondly, aldosterone levels are also frequently elevated in PCOS, which may be associated with the inflammatory state and may be involved in the pathogenesis of metabolic and cardiovascular diseases. The risk of miscarriage is increased in patients with PCOS during the early stages of pregnancy, where hyperinflammatory uterine symptoms may also contribute to a range of pregnancy complications [8].

2.5. Dysbiosis

The intestinal microbiota is known as the “second brain” of the human body and plays an important role in digestion, metabolic regulation and intestinal barrier function. On the one hand, it has been shown that the intestinal flora of normal-weight PCOS patients, PCOS with insulin resistance (PCOS-IR) patients, and healthy control women were analyzed by 16S rDNA sequencing, and it was found that the relative abundance of certain genera of bacteria (e.g., Rothia, Ruminococcus, and Enterococcus) was significantly higher in PCOS-IR group than that of the other groups, while the abundance of Prevotella was significantly lower, with Prevotella being significantly lower. other groups, while the abundance of Prevotella was significantly lower, where the abundance of Enterococcus was positively correlated with waist circumference, hip circumference, diastolic blood pressure, and insulin resistance index, and there is still a correlation between the fractionalization of intestinal flora and insulin resistance [9]. On the other hand, gut microbial communities play an important role in both obesity and PCOS, for example, a decrease in short-chain fatty acids (SCFAs) may lead to a decrease in leptin levels, which accelerates obesity. Meanwhile, if the intestinal flora dysbiosis also affects the metabolism of PCOS patients through some signaling pathways, which triggers a series of complications, so the changes of the intestinal flora components may exacerbate the symptoms of obesity and PCOS to a certain extent [10].

Dysbiosis of the gut flora may ultimately influence the development of PCOS by affecting the metabolic health of the host, which in turn affects insulin resistance, inflammatory response, and hormone levels. Dysbiosis may lead to impaired intestinal barrier function, increase penetration of endotoxins (e.g., lipopolysaccharide LPS), promote the development of obesity, and trigger a systemic inflammatory response. It also affects hormone metabolism and signaling, thereby influencing ovarian function and the menstrual cycle [11].

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2.6. Genetic factor

Among the internal factors mentioned above, such as insulin resistance, hyperandrogenemia, and chronic inflammation, these symptoms are expressed through cellular signaling molecules as well as some metabolites that go on to activate specific genes. And epigenetic processes regulate the expression of PCOS susceptibility genes by altering chromatin structure, thereby linking environmental and lifestyle factors to gene expression. For example, hypomethylation of the LHCGR gene may lead to increased sensitivity to luteinizing hormone (LH), which promotes ovarian androgen production [12].

There are studies evaluating the genetic mechanisms underlying the expression of metabolic, reproductive, and lifestyle factors associated with PCOS. Among them are the identification of multiple genes from the fetal origins of PCOS that play a role in organ development. Under the influence of genes, insulin resistance may also be associated with impaired P13K signaling, and inflammatory disorders and glucolipid metabolism are also relevant [13].

3. The role of dietary interventions

3.1. Low glycemic index diet

A low glycemic index (LGI) diet is one in which the population chooses foods with a low glycemic index, which release glucose at a slower rate during digestion and, by slowing down the digestion of carbohydrates, help to reduce postprandial blood glucose spikes and control insulin secretion. It has been shown that the LGI diet improves insulin resistance and glucose metabolism, and that controlling blood glucose and carbohydrate intake has a positive effect on improving PCOS symptoms.The ameliorative effects of the LGI diet on PCOS have been broadly categorized into four areas.First, the LGI diet, by reducing the intake of fast-acting carbohydrates, is currently being recommended for the improvement of insulin sensitivity and reproductive function, as well as for the possible improvement of PCOS-related symptoms. Second, the LGI diet may help restore menstrual regularity in PCOS patients. Next, the dietary pattern may also reduce levels of inflammatory markers in PCOS patients [14]. Finally, the LGI diet may improve reproductive hormone levels in patients with PCOS by lowering testosterone and FAI, and may improve metabolic disorders by modulating intestinal flora.

In an intervention study, the LGI diet was found to have similar improvements in weight and metabolic profiles in both PCOS and non-PCOS patients, with improvements in clinical and hormonal performance also seen in PCOS patients. Participants tolerated the LGI diet well and had high dietary adherence [15]. The importance of the LGI diet may be considered in the management of patients with PCOS, but large-scale trials and sufficient research data to comprehensively evaluate the effects of the LGI diet in PCOS are still lacking.

3.2. The Mediterranean Diet (MD) and PBDs

The MD is based on whole grains, plant foods rich in olive oil, fish and nuts, with a low intake of red meat and processed foods, and has anti-inflammatory and antioxidant properties. It has been found to reduce testosterone levels and improve menstrual cycle and ovulatory function in patients with PCOS, but the MD is low in protein intake, which may have an impact on ovarian reserve function. The MD may improve reproductive and metabolic disorders in patients with PCOS, but its dissemination outside of the Mediterranean region is challenging.

PBD is based on legumes, which are rich in fiber, protein, and minerals, and has potential for metabolic modulation. PCOS patients are often associated with metabolic syndrome and associated cardiovascular disease risk, and some findings suggest that the PBD group can be effective in improving the metabolic health of PCOS patients compared to therapeutic lifestyle change diets (TLC

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diets), especially in the controlling insulin resistance and blood lipids. Meanwhile, PBD can improve cardiometabolic indexes in PCOS patients, but its effect on reproductive function in PCOS patients still needs to be further studied [16].

3.3. Supplement management

3.3.1. Inositol and vitamin D supplements

Inositol and vitamin D supplements may help improve symptoms in patients with PCOS, including regulating hormone levels and improving insulin sensitivity, with inositol being particularly effective. Vitamin D is involved in regulating female reproductive development and influencing sex hormone synthesis. Whereas PCOS patients often have vitamin D deficiency associated with the characteristics of the metabolic syndrome, vitamin D supplementation may improve insulin resistance and reduce AMH levels by modulating insulin signaling pathways and inflammatory responses [17].

Inositol is a sugar compound, and there are nine different stereoisomers of inositol, of which Myo-Inositol (MI) and D-chiro-Inositol (DCI) have shown positive effects in the treatment of PCOS. Both act as second messengers in the insulin signaling pathway and are involved in the regulation of a variety of physiological processes [18].MI is a precursor of inositol trisphosphate, which is mainly involved in the regulation of the activities of various hormones such as TSH, FSH, and insulin, while DCI is converted to MI by insulin-dependent enzymes, which are involved in glucose uptake and glycogen synthesis [19].

MI is more effective than DCI in improving egg quality and promoting ovulation in PCOS patients. Also, MI supplementation improves BMI, insulin resistance, AMH levels and menstrual flow, corrects menstrual irregularities and normalizes ovarian volume in PCOS patients. Studies have shown that the MI/DCI ratio is critical for the treatment of PCOS, and that under normal physiologic conditions, the ratio of MI to DCI is approximately 40:1. combination therapy using MI and DCI at a ratio of 40:1 has been shown to be effective in improving ovarian function and fertility in patients with PCOS. Meanwhile, DCI has been found to increase androgen levels, which may pose a risk of further deterioration of ovarian function at high doses [20]. MI, as a safe, cost-effective, and easy-to-administer treatment without major side effects, can improve endocrine problems in patients with PCOS without affecting fertility, making it a promising option for the treatment of PCOS.

3.3.2. Probiotics

PCOS is associated to some extent with gut microbiota dysbiosis, and probiotic supplementation has in turn been suggested to potentially improve PCOS symptoms by modulating the gut microbiota. One study used a double-blind randomized controlled trial of probiotic supplementation to significantly increase sex hormone-binding globulin (SHBG) levels in patients with PCOS, but there was no significant effect on other hormones or clinical manifestations [21]. Furthermore, in probiotic supplementation, kefir fermented milk significantly improved quality of life and inflammatory marker levels in PCOS patients by modulating the gut microbiota [22]. From this, it can be found that probiotic supplementation may be beneficial for certain hormonal markers in PCOS patients, but studies with longer duration and larger sample size are needed to further confirm its effect.

3.3.3. Cinnamon and ginger

Cinnamon and ginger are thought to have anti-inflammatory and anti-hyperglycemic properties that may be beneficial in PCOS. In randomized, double-blind controlled trials, cinnamon and metformin effected the same significant reductions in insulin resistance and testosterone levels, with significant differences compared to the placebo group. In contrast, ginger significantly reduced FSH and LH

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levels, but had no significant effect on testosterone levels [23]. Cinnamon and ginger may be used as alternative treatments for PCOS, but further studies are needed to confirm their long-term effects.

4. Exercise interventions

Exercise interventions can be categorized into three types: aerobic exercise, resistance exercise, and high-intensity interval training that combines the two. In lower intensity, longer duration aerobic exercise, the body is able to effectively promote fat burning, while also improving the body's cardiorespiratory fitness. While resistance exercise is to fight against resistance to build muscle strength and endurance, the combination of the two high-intensity interval training is a combination of high-intensity bursts and short breaks in the training mode, can enhance muscle strength and burn a lot of calories in a short period of time, PCOS patients can freely choose to exercise according to their own conditions and preferences [6]. Regular exercise habits can be effective in improving physical condition. Some studies have found that 30-60 minutes of exercise per day and 75 minutes of high-intensity or 150 minutes of moderate-intensity exercise per week are recommended [24].

Exercise interventions are an important part of PCOS management and can alleviate the symptoms of PCOS by improving cardiovascular health and insulin sensitivity and regulating changes in androgen levels. Exercise interventions are also recommended to improve the metabolism of PCOS patients.

5. Conclusion

This review focuses on the detailed pathogenesis of PCOS, from the most basic insulin resistance reanalyzed to the pathogenesis of the interaction between obesity and inflammation, while mentioning the influence of gut microbiota on patients with PCOS, as well as the hidden genetic factors. Both dietary and exercise interventions mentioned in the paper can be effective tools in the management of patients with PCOS. Dietary interventions focus on regulating insulin sensitivity and lipid health through diet. While exercise intervention improves physical fitness and metabolism. Through the research in this paper, understanding the more comprehensive pathogenesis of PCOS, combined with the current representative dietary interventions and exercise interventions, can provide effective suggestions for the management of PCOS patients, in order to better improve the physical condition. However, in the course of continuous research, the authors found that most of the effects on the management of PCOS have not been referenced by larger-scale objective experimental data, and there are still some unclear boundaries regarding physiologic changes in PCOS that need to be addressed. In future studies, with a deeper understanding of PCOS, the diagnostic criteria will be updated, the impact of dietary interventions will be verified and appropriate dietary intervention strategies will be developed taking into account different ethnic and cultural backgrounds, and exercise interventions will be further investigated to determine the optimal type and intensity of exercise. In the future, the combination of different interventions will also establish an effective and healthy management for PCOS patients.

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