

The Therapeutic Effect of Mediterranean Diet Intervention on Patients with Polycystic Ovary Syndrome at Different Ages

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Abstract. Polycystic ovary syndrome (PCOS) is a common and morphologically diverse endocrine disease that is affecting the quality of life, reproductive function and long-term health of 6%-20% of women worldwide. PCOS treatment prefers healthy lifestyle guidance, and diet control is an important part of it. At present, there is not enough evidence that any special diet type is better. Some studies show that the Mediterranean diet (MD) can improve indicators such as the physical indices, reproductive endocrine function, degree of insulin resistance, and blood lipid profiles of PCOS patients. However, at present, the coherresistence between MD and PCOS is rarely systematically combed or analyzed. This article analyzes the therapeutic effect of MD on PCOS patients in adolescence and childbearing age. It is found that MD has a positive impact on PCOS patients in adolescence in terms of weight management, improving appearance/promoting mental health, etc. For PCOS patients of childbearing age, it can also regulate hormone levels, improve fertility and improve pregnancy. Moreover. However, the treatment effect of MD on PCOS of different ages still lacks direct evidence support such as imaging. In addition to providing scientific and theoretical reference for the future development of PCOS treatment, this study also hopes that future research can pay more attention to the use of imaging evidence in therapeutic effect.

Keywords: Polycystic ovary syndrome, mediterranean die, age-specific treatment.

1. Introduction

Polycystic ovary syndrome (PCOS) is a prevalent and morphologically diverse endocrine disease. Its characteristics include excessive androgen levels, persistent anovulation, and ovarian polycystic changes. Conservative estimates indicate that the prevalency of PCOS among women of childbearing age ranges from 6% to 15%. Additionally, 50% to 70% of PCOS patients suffer from insulin resistance (IR), with obese PCOS patients making up approximately 75% of those with IR. The negative consequences of many PCOS are mainly due to decreased insulin sensitivity and high levels of androgens [1]. Research shows that nearly 35% of overweight PCOS patients will develop metabolic syndrome (prediabetes); 10% will develop type 2 diabetes (T2DM). In addition, the prevalencyof female infertility in PCOS is 15 times that of normal women. Irregular or missing menstrual cycles, as well as adverse results in newborns and pregnancy, are also closely related to

this [2]. The disease can affect women's quality of life, reproductive function and long-term health, and requires active treatment and long-term management.

The treatment of PCOS should first be based on healthy lifestyle guidance. The basic treatment of PCOS patients advocated by domestic and foreign guidelines is lifestyle intervention, and diet control is an important part of it. The consensus of experts on the diagnosis and treatment path of PCOS recommends eating more unsaturated fatty acids, while consuming abundant vitamins, minerals and dietary fiber to change bad eating habits. However, the guideline also points out that there is not enough evidence that any special diet type is better.

With the continuous progress of research, the Mediterranean diet (MD) has become a highly respected diet structure. Its nutritional structure recommends whole grains as staple food, emphasizing the intake of numerous vegetables, beans and nuts, fish and seafood, and recommending the use of vegetable oils containing unsaturated fatty acids, especially olive oil.

Some studies show that MD can improve indicators such as physiological indices, gonadal hormone profiles, insulin sensitivity markers, and lipid metabolism parameters of PCOS patients [1]. However, at present, the relationship between MD and PCOS is rarely systematically sorted out or analyzed. Therefore, this article intends to clarify the effect of MD on the treatment of PCOS, aiming to provide scientific and theoretical reference for the treatment of PCOS.

2. PCOS

2.1. The epidemiological characteristics of PCOS show three highs and one low

The epidemiological manifestations of PCOS are characterized by high incidence, high proportion of androgenemia, high proportion of stimulating metabolic syndrome and low attention. It is widely believed that the incidence of PCOS is as high as 6~20%, and the incidence of adolescents has shown an upward trend in recent years, which shows that it poses significant hazard to the endocrine metabolic well-being of females worldwide. Approximately 85% of individuals with PCOS suffer from hyperandrogenemia, with distinct clinical presentations including visible cosmetic alterations like hirsutism, acne, and alopecia, which are directly linked to abnormal androgen secretion from the ovaries and adrenal glands. Additionally, those with PCOS face an elevated risk of metabolic disorders compared to the general female population. The consensus of the International Diabetes Federation (IDF) shows that the high incidence of T2DM and cardiovascular disease (CVD) is the most significant. About 40% of PCOS patients suffer from T2DM or impaired glucose tolerance at the age of 49. And the incidence of metabolic syndrome is 3-5 times higher than that of the general population. In addition, metabolic abnormalities (such as obesity and insulin resistance) persist in postmenopausal PCOS patients, resulting in increased difficulty in diagnosis and prolonged treatment time. In addition, the clinical symptoms of PCOS are highly specific, requiring long-term management and the therapeutic effect varies from person to person. Patients are prone to delay intervention due to lack of confidence in treatment or lack of awareness of the disease, which shows that the current degree of attention is low.

2.2. Risk factors of PCOS

PCOS has significant genetic predisposition and familial clustering. The risk of disease among the patient's immediate relatives is 2-3 times higher than that of the general population. At the same time, it is also affected by key genetic mutations and genetic and environmental interactions. As the core mechanism and characteristic of PCOS, metabolic abnormalities occupy an important position

in the pathogenesis. The New England Journal of Medicine pointed out that Insulin resistance lies at the heart of the incidence of PCOS. About 60-70% of PCOS patients have insulin resistance, which is manifested as increased fasting insulin levels and abnormal glucose tolerance, and hyperinsulinemia will further stimulate androgens. Synthesis and secretion aggravate the disease. At the same time, about 50-70% of PCOS patients have obesity symptoms, and abnormal fat distribution will aggravate insulin resistance and hyperandrogenemia; PCOS patients are often accompanied by lipid metabolism disorders, which increases the risk of atherosclerosis. Insulin resistance and obesity will also increase the level of oxidative stress in the body and promote the release of inflammatory factors, thus forming a vicious circle of metabolic abnormalities and inflammation.

3. MD

3.1. MD composition and characteristics

The MD is mainly composed of whole grains and beans, vegetables and fruits, healthy fat and high-quality protein. It is characterized by less processing of high-fresh ingredients and a balanced diet structure. This diet model emphasizes the intake of a large amount of fruits and vegetables, whole grains, beans and other plant foods. Fat sources replace saturated fat with unsaturated fatty acids, and protein is mainly fish, seafood and other animal proteins rich in Omega-3 fatty acids. Because the md diet pattern has been proven to reduce the risk of CVDs, metabolic diseases (such as diabetes, obesity) and some cancers, it has gradually sublimated from a regional diet to a globally recognized healthy diet model.

3.2. The relevant mechanism of MD's action on metabolic diseases

Predimed's clinical study shows that the MD can reduce the risk of T2DM by 52% and significantly reduce abdominal fat. MD can improve insulin sensitivity, monounsaturated fatty acids reduce liver fat accumulation by enhancing insulin signaling; high dietary fiber reduces postprandial blood glucose fluctuations by delaying glucose absorption. Md also has anti-inflammatory and antioxidant effects. By reducing oxidative stress, it reduces inflammatory markers, regulates immunity to suppress inflammation, and can also improve insulin resistance with chronic inflammation. In addition, md regulates body weight and fat distribution, and foods with high fiber and low energy density reduce total energy intake by 10-15%; increasing the level of adipose can improve adipose tissue function.

3.3. The specific impact of characteristic nutrients on metabolic pathways

MD regulates the body's metabolic pathway through a variety of key components. Monounsaturated fatty acids in olive oil can activate the PPAR- γ pathway, enhance insulin sensitivity and reduce liver fat accumulation, and optimize blood lipid spectrum. The American Diabetes Association (ADA) recommends it as the main fat source. Omega-3 fatty acids in deep-sea fish and nuts reduce TNF- α , IL-6 and other pro-inflammatory factors by inhibiting the NF- κ B pathway, improving insulin resistance, and reducing VLDL synthesis to reduce triglyceride levels. Polyphenolic compounds enhance antioxidant enzyme activity by activating the Nrf2 pathway, reducing oxidative stress, and inhibiting inflammatory media such as COX-2; plant-based phenolic compounds can regulate the action and metabolism of insulin in insulin-sensitive tissues. High dietary fiber foods (whole grains, beans) are fermented to generate short-chain fatty acids (SCFAs), which stimulate glucagon-like

peptide-1 (GLP-1) secretion via GPR41/43 receptors, improve sugar metabolism, and optimize the structure of intestinal flora. Plant sterols such as nuts can competitively inhibit cholesterol absorption and reduce LDL-C by 10-15%. The MD can reduce the risk of CVD by 24.7%-28.1% and significantly improve metabolic health. The predimed study confirmed that this diet pattern reduced the incidence of T2DM by 52%, while the green MD performed better in weight resumption and improved cardiovascular indicators. The MD Guide released by the Italian Institute of Health in 2025 is based on 40,000 studies, emphasizing it as an evidence-based strategy for the management of metabolic diseases.

4. The influence of MD on adolescent PCOS

4.1. Improve metabolism

MD can effectively improve the metabolic status of PCOS teenagers. A study recruited 40 15-17-year-old PCOS adolescents who were randomly divided into the MD group and the control group. The MD group received a tailored MD diet plan through the Clinical Decision Support System (CDSS). Findings indicated that the MD group had lower intake of energy, total fat, saturated fat, and cholesterol, alongside higher intake of monounsaturated fat and fiber, and serum calcium and vitamin D levels are improved; and a comparative study of normal and overweight adolescent girls on the clinical characteristics of PCOS shows that Cholesterol consumption was positively correlated with CRP ($r = 0.342$, $p = 0.038$). Anti-inflammatory diet (AIDiet) follows the MD principle without limiting energy intake. After 12 weeks of AIDiet intervention on adolescent PCOS girls, it was found that the KIDMED score was significantly improved, reflecting the improvement of compliance and total antioxidant ability (TAC), fasting insulin, insulin resistance index (HOMA IR) improved significantly; a study by Violi et al. on obese PCOS patients also found that patients who adhered to MD showed a significant decrease in fasting blood glucose and insulin levels after 12 weeks, while HOMA-IR index has also improved. In addition, the study of Neyrinck and others showed that the high fiber content of MD further improved the composition of intestinal flora by increasing the production of SCFAs, thus indirectly regulating insulin sensitivity [3-6].

4.2. Reduce the inflammatory factor

MD can also reduce the inflammatory factor of PCOS adolescents. Chronic low-grade inflammation is one of the core pathological characteristics of PCOS, and the research of Khashchenko and others points out that the level of inflammatory markers (such as CRP) in overweight/obese PCOS girls is relatively high. At the same time, the intake of macronutrients in adolescents of PCOS patients. Studies on the relationship with inflammation and oxidative stress found that plant protein intake was associated with inflammatory indicators, and the study of Mizgier et al. showed that the intake of vegetable protein, carbohydrates and fiber was inversely associated with markers of inflammation and oxidative stress in overweight or obese adolescent patients with PCOS, such as IL-6, TNF- α and MDA, which indicate that MD may exert a beneficial impact on the inflammatory state of adolescent PCOS, because MD emphasizes the intake of a large amount of vegetable protein and can restrain the secretion of pro-inflammatory adipocytokines through the reduction of visceral fat; in addition, Tsigalou et al. (2020) found that MD reduced the release of pro-inflammatory cytokines by regulating the intestinal flora, while increasing the level of anti-inflammatory factors such as adiponectin. In the intervention study of AIDiet on adolescent PCOS girls, it was also found that post-interventional inflammation. The concentration of symptomatic factors such as interleukin (IL)-1, IL-

6, tumor necrosis factor (TNF)- α and androgens decreased. Although the sample size is relatively small, the study of Mizgier and others also found that through AI-assisted diet intervention, the inflammatory status of PCOS adolescents and the composition of the body has been improved [7-9].

4.3. Mental health

Although there is little direct research on the impact of MD on the mental health of PCOS adolescents, the metabolic and anti-inflammatory benefits of MD may indirectly improve the psychological state. In the study of Gorska et al., the antioxidant components in MD (such as olive polyphenols) may exert a beneficial effect on cerebral function by mitigating oxidative stress, thereby enhancing mood and cognitive performance. In a study by Foscolou et al., a 3-month personalized MD plan was provided to 40 15-17-year-old adolescent PCOS women. After the intervention, it was found that the MD compliance of the group was significantly improved with the control group; the anxiety score of the MD group decreased from 8.5 to 4.1, and the data of the control group showed No statistical significance. In addition, MD emphasizes high-quality fat intake, and Fatemi et al.'s study found that high-quality dietary fat intake is negatively correlated with women's anxiety levels. At the same time, the research of López-García and others shows that the dietary fiber rich in MD can regulate the intestinal flora, and there is a two-way signaling pathway between the intestinal flora and the brain. This regulatory effect may indirectly improve the emotional state through the "intestinal-brain axis" and provide the positive impact of MD on mental health. A new potential mechanism [3,10].

5. The impact of MD on PCOS during childbearing age

5.1. Improve metabolism

MD has a positive effect on improving the metabolism of patients with PCOS. Song Guanshu and others carried out a 12-month MD intervention on 120 pregnant women with PCOS, including 62 cases in the intervention group and 58 cases in the control group. The results showed that fasting blood sugar decreased from 8.40 mmol/L to 5.06mmol/L after 3 months of intervention; body fat percentage (BFP) and subcutaneous Fat thickness (SFT) decreased from 35.38% and 29.76 mm to 33.60% and 26.93 mm respectively after 6 months of intervention; total cholesterol, triglycerides and low-density lipoprotein decreased from 4.63mmol/L and 2.11 mmol/ L, 3.21 mmol/L reduced to 3.58 mmol/L, 1.65 mmol/L, 1.39mmol/L [11]. Xu Li and others conducted a 12-week intervention study on 64 obese PCOS patients (BMI 25~45 kg/m²). The experimental group adopted a MD and walking exercise. The results showed that the weight of the experimental group decreased from 75.39kg to 66.42kg, and the BMI decreased from 28.10 to 24.73, both of which were significantly better than the control group [12]. Meneghini et al. conducted a non-randomized controlled study of 84 overweight/obese PCOS patients (BMI > 24.9 kg/m²), which was divided into MD group and extremely low-calorie ketogenic diet (VLCKD) intervention. 13.57 mg/dL decreased, and the HOMA index (insulin resistance marker) decreased by 0.33 [13]. Mei et al. divided 72 overweight PCOS patients of childbearing age into MD combined low-carbohydrate diet group (MD/LC) and low-fat diet group (LF). After 12 weeks of intervention, it was found that the MD/LC group exhibited significantly greater improvements than the LF group in terms of weight, BMI, waist circumference, body fat percentage, fasting insulin, HOMA index, and blood lipid levels. The weight of the MD/LC group and bmi low-lipid group were about 1.3 times, and the insulin resistance index was reduced by 2 times [14]. A study conducted by Barrea and colleagues compared

112 adult females with PCOS and 112 healthy control subjects. Results revealed that females with PCOS had a higher fat mass, and adherence to the MD was inversely correlated with testosterone levels; while the daily diet structure was closer to the MD of PCOS patients, the serum testosterone was lower and the hisutism was lighter [7].

5.2. Regulate hormone levels

MD plays an active role in adjusting the hormone levels of PCOS patients of childbearing age. Song Guanshu and others conducted a 12-month MD intervention study on 120 PCOS pregnant women and also found that the level of luteinizing hormone (LH) in the intervention group dropped from 10.04mIU/mL to 8.71mIU/mL after 3 months of intervention, and further to 5.71mIU/mL after 6 months. U/mL ($P<0.05$); Although there is no significant change in the FSH level, the decline in the LH/FSH ratio suggests that the endocrine environment tends to be balanced. The review of Artini and others also pointed out that the MD can improve the ovulation function of patients with PCOS by regulating LH levels [11]. According to the study of Xu Li and others, after 3 months of MD intervention on 20 patients with PCOS of childbearing age, it was found that the levels of LH and LH/FSH of these 20 women decreased significantly [15].

A study by Yang et al. found that in seven randomized controlled trials (RCTs) involving the MD and the control diet, the MD reduced the risk of gestational diabetes, and the relative risk (95% confidence range) was 0.74 (0.55 - 0.99); in terms of fertility, although the specific data for PCOS patients was not clear, it showed that the MD had a positive correlation with fertility and pregnancy weight management [16]. The study of Mei et al. found that while MD can effectively improve the metabolic effect of PCOS patients, it also shows that the testosterone and LH levels of the MD group decreased and the SHBG levels increased, indicating that it also has a promoting effect on the regulation of patients' hormone levels [14]. In the study of Meneghini et al., the level of anti-Muller's hormone (AMH) in the MD group decreased from 6.08 ng/mL to 4.70 ng/mL, and the testosterone level decreased from 1.76 nmol/L to 1.64 nmol/L. In addition, the FSH/LH ratio was reduced from 1.10 to 0.95, indicating that MD helps to improve the hypothalamic-pituitary-ovarian axis function of PCOS patients [13].

5.3. Improve fertility function

MD can significantly improve the probability of IVF pregnancy and natural conception rate of PCOS women. In the study of Xu Li and others, after 3 months of MD intervention on 20 patients with PCOS of childbearing age, it was found that 16 of these 20 women returned to normal menstruation and 9 of them were successfully pregnant. The PCOSQ score of the experimental group increased from 2.27 to 4.44 in the "infertility" dimension, which is significantly higher than that of the control group [15]. Although the study of Song Guanshu and others did not directly statistics the conception rate, The abortion rate in the intervention group (6.45%) was significantly lower than that in the control group (17.24%), which indirectly reflected the improvement of reproductive function [11]. In a study of 161 couples treated with IVF/intrapollasmic single sperm injection (ICSI), higher MD compliance before treatment was associated with a higher probability of pregnancy after IVF [17]. The research of Gitsi and others shows that a highly compedient MD is associated with the improvement of natural conception and clinical pregnancy, and can indirectly promote reproductive health. In the study of Meneghini et al., the improvement rate of menstrual regularity in the MD group stood at 26%. In comparison with the VLCKD group, the mild diet of MD was more suitable for long-term persistence. In addition, the sinus follicle count (AFC) of the

MD group decreased from 18.33 to 15.38, indicating an improvement in ovarian function [13]. Another study by Mei et al. showed that MD combined with a low-carbohydrate diet (MD/LC) significantly improved the ovulation rate and reduced LH and testosterone levels in 72 overweight PCOS patients, further supporting the role of MD in improving reproductive function. Excessive testosterone levels can lead to menstrual irregularities, infertility and other abnormalities in women. Barrea et al.'s research found that MD compliance is negatively correlated with testosterone levels in PCOS women [7].

5.4. Improve pregnancy

MD can significantly reduce the incidence of pregnancy complications in patients with PCOS of childbearing age, improve pregnancy, and reduce adverse outcomes. According to the research of Song Guanshu and others, the incidence of pregnancy complications in the intervention group was significantly lower than that of the control group: gestational hypertension (8.06% vs 18.97%), gestational diabetes (6.45% vs 22.41%), premature rupture of membranes (4.84% vs 15.52%) and premature birth (3.23% vs 15.52%); the incidence of adverse neonatal outcomes such as jaundice is also significantly reduced (3.23% vs 13.79%) [11]. The study of Yang et al. also found that in seven RCTs involving a MD and a controlled diet, the risk of premature birth was reduced, and the relative risk was 0.45 (0.26 - 0.76); the risk of hypertension during pregnancy was reduced, and the relative risk was 0.71 (0.51 - 1.00); the MD reduced the risk of gestational diabetes, and the relative risk (95% confidence interval) was 0.74 (0.55 - 0.99); the risk of preeclampsia was reduced, and the relative risk was 0.82 (0.54 - 1.22) [16].

6. Conclusion

In summary, the exploration of the MD pattern to improve the symptoms and outcomes of PCOS patients of different ages has yet to be updated. In particular, there is no direct evidence of the beneficial effect of MD on perimenopausal PCOS women, and the impact of MD on PCOS patients of different ages still needs to be followed up for a long time. For adolescent PCOS patients, MD shows a positive impact on weight management, improvement of appearance/promotion of mental health, and at the same time reflects high compliance and acceptance. It is recommended to try it. For PCOS patients of childbearing age, in addition to improving metabolic levels, MD also reflects the effect of regulating hormone levels, improving reproductive function and improving pregnancy, but for PCOS patients in non-Mediterranean areas, compliance is low. In addition, MD's treatment effect on PCOS of different ages still lacks direct evidence support such as imaging. In addition to providing scientific and theoretical reference for the future development of PCOS treatment, this study also hopes that future research can pay more attention to the use of imaging evidence in therapeutic effect.

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