The Therapeutic Effect of Mediterranean Diet Pattern on Overweight/obese Patients with PCOS

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Abstract. Polycystic ovary syndrome (PCOS) is a common endocrine disorder in women of childbearing age, and nearly half of women with PCOS exhibit overweight or obesity. The vicious cycle of hyperandrogenemia (HA), insulin resistance, and obesity symptoms in overweight/obese PCOS patients seriously affects their physical and mental health. Mediterranean diet (MD), as one of the healthy dietary patterns, is gradually attracting attention. After a comprehensive analysis of the therapeutic effects and current research progress of the MD on overweight/obese PCOS patients, this article found that the MD pattern uses foods such as soybeans, fish, olive oil, almonds, walnuts, etc. to regulate various physical and chemical factors in the body and improve the related symptoms associated with PCOS patients. At the same time, it is proved that MD mode can reduce the long-term disease risk of PCOS such as cardio cerebrovascular disease, type 2 diabetes (T2D) and fatty liver to a certain extent. In addition to single use, the lifestyle intervention of MD combined with physical exercise can also improve the therapeutic effect. However, there are still limitations in the application and research progress of the MD model in China, and further exploration is needed to choose personalized dietary models.

Keywords: Polycystic ovary syndrome; overweight/obese polycystic ovary syndrome; obesity; hyperandrogenemia.

1. Introduction

Polycystic ovary syndrome (PCOS) is a common reproductive endocrine disease in women, affecting approximately 8% to 13% of women of childbearing age worldwide, with a prevalence rate of 5.61% among Han Chinese women [1,2].The clinical manifestations of PCOS are highly heterogeneous, often with rare menstruation, amenorrhea, irregular vaginal bleeding, infertility, and accompanied by hyperandrogenemia（HA）, hyperlipidemia, insulin resistance (IR) and other clinical manifestations, which may lead to fatty liver, cardiovascular and cerebrovascular diseases, and type 2 diabetes (T2D) for a long time [3].The high incidence of PCOS seriously affects women's reproductive health, psychological status, and quality of life.

At least 50% of PCOS women exhibit overweight (BMI>25 kg/m^2) or obesity (BMI>30 kg/m^2) [4]. Compared with non-obese PCOS patients, overweight or obese PCOS patients have more severe conditions and are more difficult to successfully conceive [4]. Compared to healthy women with age and BMI matching, women with PCOS have lower intake of complex carbohydrates, fiber, and higher intake of simple carbohydrates and fats [5]. This indicates that PCOS patients themselves generally have poor dietary habits, which have become an important trigger. Obesity may exacerbate insulin resistance and dyslipidemia in PCOS patients, as well as lead to an excessive increase in androgen levels in the body. Abnormal hormone regulation is the cause of obesity; Obesity is the most common cause of insulin resistance, and excessive insulin can lead to obesity in PCOS patients, forming a vicious cycle that urgently needs attention [6].

Advocated by domestic and foreign guidelines, the basic treatment for PCOS patients is lifestyle intervention, including diversified strategies such as reasonable exercise, dietary control, and behavioral intervention.For overweight/obese PCOS patients, weight loss is the key to treatment. Changing the dietary structure can significantly improve related symptoms, such as obesity (abdominal fat accumulation), acne, hirsutism, black spiny skin, menstrual disorders, infertility, and insulin resistance.In recent years, various dietary patterns have been utilized to treat PCOS. However,

different dietary interventions have varying effects on endocrine and metabolic indicators, sex hormone indicators, ovulation, and pregnancy in PCOS women. Currently, there is no optimal dietary pattern proposed.

The Mediterranean diet (MD) is a world intangible cultural heritage that has been well-known in the Mediterranean coastal areas since the 1960s.In recent years, as one of the healthy diets, MD is very popular and plays an important role in the prevention and treatment of cardiovascular diseases, T2D, dementia and cancer [7].With the continuous deepening of research, there are also studies indicating that MD plays a role in the treatment of PCOS, such as improving dietary structure, regulating metabolic balance in the body, or maintaining a good mentality.This article aims to summarize and analyze the effect of MD on the treatment of obese POCS based on previous research on the dietary pattern for treating PCOS. To provide a certain reference basis for clinical intervention in PCOS, improvement of patient lifestyle, and selection of personalized dietary patterns.

2. Mediterranean Diet (MD)

MD is a traditional dietary pattern unique to residents of southern European countries along the Mediterranean coast that originated in the 1970s [8].The Mediterranean is located between Europe, Africa, and the Asian continent, and is mostly composed of European countries. The main representative countries of its dietary pattern include France, Italy, Greece, Spain, etc.MD mainly focuses on vegetables, fruits, legumes, grains, seeds, fish, nuts, and olive oil. Its food processing is very simple, based on plant-based foods, with vegetable oil and nuts as the main sources of fat, white meat replacing red meat, and moderate dairy products and moderate amounts of wine as supplements. MD is characterized by being simple, light, and nutritious, with a dietary structure of high fiber, high vitamins, low fat, and low-calorie intake.

3. The Therapeutic Effect of MD on Overweight/obese PCOS

3.1. Improving Obesity Symptoms

MD, as one of the popular healthy dietary patterns among weight loss individuals, may also have a good weight loss effect on overweight/obese PCOS, thereby improving the obesity symptoms. A randomized controlled study included 72 overweight PCOS patients who were randomly divided into a MED/LC (MD combined with low carbohydrate) diet group (n=30) and a low fat (LF) diet group (n=29) for 12 weeks of intervention [9]. The body weight, BMI, waist to hip ratio (WHR), body fat percentage (BF%), and various metabolic indicators of the two groups were compared before and after intervention. The results showed that compared with the MED/LC group, the weight loss trend (-6.10 vs. -4.79), BMI decrease trend (-2.12 vs. -1.78 kg/m^2), WHR decrease trend (-0.06 vs. -0.03), and BF% decrease trend (-2.97% vs. -1.19%) in the LF group were more significant ($P<0.05$ or $P<0.001$), fully confirming that the combination of MD mode and low carbohydrate diet can help overweight PCOS patients lose weight and improve obesity symptoms.At the same time, the obesity and insulin resistance of PCOS patients form a vicious cycle with Kaohsiung, and improving the Kaohsiung and insulin resistance of PCOS can also have an effect on improving obesity.

3.2. Regulating the Balance of Hormone Levels

HA is a major feature of PCOS, with 60% of PCOS patients also suffering from it. The characteristics related to HA often include hirsutism, acne, and black prickly skin.Animal experiments have shown that androgens participate in the occurrence of PCOS through the mediation of androgen receptors (AR).PCOS patients are often accompanied by HPO axis disorder, abnormal secretion of GnRH, increased pituitary sensitivity, and the release of more luteinizing hormone (LH). Excessive LH and receptor binding promote excessive secretion of androgens by granulosa cells in the follicular membrane. At the same time, follicle stimulating hormone (FSH) is relatively insufficient, and androgens in granulosa cells cannot be converted into estrogen, ultimately leading

to excessive androgens, affecting follicular development or maturation, resulting in anovulation or small follicle development. Excessive estrogen is generated without the antagonistic effect of progesterone, and the endometrium continues to proliferate and cannot shed, ultimately resulting in infrequent menstruation or amenorrhea. Multiple studies have shown that MD may effectively reduce the LH levels, thereby lowering androgen levels and restoring normal menstruation in PCOS patients [10].

Plant based foods, such as peanuts, soybeans, and other soybean-based foods, which are the main sources of MD dietary patterns, can stimulate the synthesis of SHBG (sex hormone binding globulin) in the liver during their growth process, which can bind with active free androgens in the body, thereby reducing the level of free androgens and achieving the effect of male reduction [11].

Fish and olive oil contain a large amount of unsaturated fatty acids (UFA). A randomized controlled study included 78 overweight/obese PCOS patients, who were randomly divided into an experimental group+omega-3 (n=39) and a control group+placebo (n=39) [12]. After an 8-week trial, the serum testosterone concentration, menstrual cycle, and free androgen index of the two groups were compared before and after treatment. The results showed that the serum testosterone concentration in the experimental group was lower than that in the control group (0.25 vs. 0.3, p=0.04); The percentage of menstrual patterns in the experimental group was significantly higher than that in the control group (47.2% vs. 22.9%, p=0.049),indicating that supplementing Omega-3 fatty acids, one of the components of UFA, can reduce androgen levels and regulate the menstrual cycle. However, the experimental results showed no significant difference in the changes in SHBG concentration and free androgen index, indicating the need for longer intervention.

Another study included 31 PCOS patients who were randomly assigned to walnuts or almonds containing 31 grams of total fat per day [13]. After 6 weeks, data on fasting lipids, phospholipid fatty acids, and androgen levels were obtained from the study subjects. The results showed that walnuts increased sex hormone binding globulin from 38.3 to 43.1 nmol/l (P=0.0038), while almonds decreased the free androgen index from 2.6 to 1.8 (P=0.0470); And walnuts lower density lipoprotein cholesterol and low-density lipoprotein, which indicates that the intake of nuts has beneficial effects on plasma lipids and androgens in women with PCOS. Walnuts can increase sex hormone binding globulin (SHBG), while almonds can reduce free androgens (FT). Both can improve metabolism in women with PCOS to exert anti androgenic effects.

Meanwhile, PCOS with HA may lead to infertility. In an 8-year observational study of 17544 women of childbearing age without a history of infertility, it was found that adhering to a diet pattern similar to MD (high unsaturated fat, plant protein, low carbohydrates, high-fat dairy products, multiple vitamins, and plant-based foods, etc.) is closely related to reducing ovulation disorders and infertility, thus proving that dietary intervention can to some extent assist in solving the problem of pregnancy preparation in PCOS patients of childbearing age [14].

3.3. Improving Insulin Resistance

MD may significantly reduce the insulin levels. A randomized controlled study included 102 Chinese patients with PCOS, who were randomly divided into a targeted dietary intervention group (control group,n=51) and a routine care intervention group (study group,n=51) [15]. Patients were followed up regularly after leaving the hospital to observe and compare their dietary compliance, insulin resistance levels, fasting insulin levels, quality of life scores, and sex hormone levels before and after nursing care. The results of the intervention showed that the dietary compliance and quality of life scores of the intervention group were significantly higher than those of the control group (P<0.05). The intervention group had significantly lower BMI (23.01 vs. 24.36), fasting insulin (12.87 vs. 17.37), insulin resistance (2.27 vs. 3.06), T (serum testosterone) (1.25 vs. 3.02), FSH (2.72 vs. 10.69), LH levels (6.58 vs. 4.11) than the control group (P<0.05).The result Indicates that targeted dietary interventions can significantly improve various indicators such as BMI, insulin resistance levels, and sex hormone levels in PCOS patients.Among them, dietary intervention guides patients to consume more vegetables and coarse grains, choose low sugar fruits, high-quality protein, avoid

animal fats, and have a light diet. The structure is similar to the MD and has reference value.In addition, vegetables, fruits, and grains in MD are rich in dietary fiber and vitamins, which can increase satiety. Rich dietary fiber can reduce blood sugar load, improve insulin sensitivity, and help patients control their diet to achieve weight loss.

3.4. The Lifestyle Intervention of MD Combined with Exercise

Dietary intervention combined with rational exercise lifestyle intervention, MD combined with daily exercise, can more efficiently treat obese PCOS.A randomized controlled trial included 66 Chinese PCOS patients with a body mass index (BMI)≥25kg/m^2 [16]. They were blinded and divided into a regular diet intervention group (control group,n=30) and a MD combined with brisk walking intervention group (study group,n=36). After two months of treatment, the endocrine hormone levels before and after the intervention were compared between the two groups. The results showed that the levels of testosterone (0.52 vs. 0.83) and insulin resistance index (4.04 vs. 5.22) in the study group were lower than those in the control group ($P<0.05$).The combination of MD and brisk walking intervention can effectively improve the endocrine hormone levels in overweight/obese PCOS patients. Research has shown that dietary intervention combined with reasonable exercise can more effectively improve symptoms in obese PCOS patients than simple dietary intervention.Therefore, it is currently advocated that medical staff provide corresponding exercise prescriptions on the basis of the MD model when treating obese PCOS, guiding patients to receive MD dietary intervention while arranging physical exercise, which can develop a good lifestyle to accelerate the pace of disease improvement and achieve a more ideal treatment effect.

Anxiety, depression, and other emotions may also exacerbate insulin resistance, leading to further deterioration of endocrine indicators and worsening of the condition. So, the therapeutic effect of lifestyle interventions for PCOS patients will also be influenced by emotions, indicating that maintaining a good psychological state can assist in improving the therapeutic effect.

3.5. Reduce Long-term Risk

Before MD became an effective choice for treating PCOS, many studies domestically and internationally have confirmed its application in improving metabolic related diseases.At first, the research was used to treat cardiovascular diseases, and then the research on diabetes, dementia and other diseases also increased. MD may prevent the occurrence of T2D and control its progress by reducing blood pressure, blood fat, weight, insulin resistance and glucose metabolism. A meta-analysis of the effect of dietary intervention on blood glucose and related factors in patients with T2D and gestational diabetes included nine studies(n=1178) [17]. The trial group used MD dietary intervention. The results showed that MD diet significantly reduced the levels of glycosylated hemoglobin, fasting insulin, and insulin resistance in T2D patients, significantly improved cardiovascular risk factors, reduced the levels of total cholesterol, triglycerides, and blood pressure, increased the level of high-density lipoprotein, all of which were better than the control group. To some extent, it indicates that MD may not only improve blood glucose metabolism in patients, but also improve cardiovascular risk factors. Meanwhile, as mentioned earlier, MD has a beneficial effect on plasma lipids, not only reducing BMI but also improving metabolism, proving its ability to prevent fatty liver in the later stage of PCOS. Therefore, it is necessary to persist in longer duration MD mode interventions.

4. Limitations of MD

4.1. Immature Research on MD in China

The research on MD is relatively mature abroad. In China, it is more limited to T2D, cardiovascular disease, dementia, etc., and there is less research on PCOS. The existing MD related research on PCOS also has problems such as the small sample size, short intervention time, and lack of long-term follow-up results. Existing scholars in our country have developed an improved MDary model by

replacing olive oil with sunflower seed oil and using walnuts as the main nut according to their own national conditions and dietary habits. This diet has been applied to pregnant women and has achieved good results, indicating that MD can also be used for intervention in other diseases. However, further clinical evidence-based studies are needed to confirm this [18].

4.2. MD Applications are not Widespread and Their Scope of Application is Restricted by the Bureau

MD is a traditional dietary model based on the lifestyle of the Mediterranean region, but it is not applicable to all regions. For example, the development of fisheries in inland areas is relatively limited, and the supply of seafood is not as good as in coastal areas. On the other hand, due to different dietary habits in different countries and regions, patients from other regions may not adapt to this dietary pattern.

5. Future Prospects of MD Dietary Model

PCOS has brought various physiological and psychological adverse effects such as HA, insulin resistance, obesity, and changes in masculinized physical signs. Medical staff should strengthen education to make patients and the entire society aware of PCOS and enhance their awareness and awareness of the disease. The concept of popularizing the MD model as one of the healthy dietary models can serve as an effective way to assist in the intervention of PCOS, fulfilling the promise of popularizing and applying MD. In the future, researchers should strengthen the exploration of the association between MD and PCOS, expand the sample size, strengthen evidence-based data, and focus on exploring the advantages brought by MD and its connection with PCOS. At the same time, it is hoped that clinical healthcare professionals can refine their food choices and develop personalized dietary interventions based on the different demands of PCOS patients with different phenotypes. For adolescent women, how to better restore menstrual cycles, and for women of childbearing age, how to better protect fertility. By optimizing and adjusting the types of food to achieve targeted treatment, the food elements in the MD model are adjusted according to different demands, solving individual problems for each patient, making the MD pattern more diversified and widely applicable.

6. Conclusion

In a word, MD has significant therapeutic effects on obese PCOS patients, to some extent, improving symptoms such as HA, insulin resistance, and obesity. The lifestyle intervention therapy of MD combined with exercise has also been recognized and applied, with good results. At the same time, a good mental state can play an auxiliary role. In addition, MD provides assistance in reducing the long-term risk of overweight/obese PCOS and mitigating disease risk.

However, there are currently problems such as limited and immature research, lack of popularization of relevant knowledge, and limited application population. In the future, researchers and healthcare professionals still need to work together to explore the relationship between MD dietary patterns and PCOS, find the best personalized dietary patterns, and strengthen the popularization of related disease knowledge and lifestyle interventions. In addition, MD originates from abroad and needs to be combined with the characteristics of Chinese dietary habits to be suitable for Chinese PCOS women. In the future, more large-scale and higher quality clinical trials are needed to evaluate the effectiveness of different dietary approaches in improving PCOS symptoms and their adjuvant therapeutic effects on long-term complications, thereby improving patient compliance.

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