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Application of Different Dietary Patterns in Hyperuricemia/Gout

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Abstract:

Hyperuricemia and gout, as common metabolic diseases, have witnessed a continuous increase in incidence in recent years, becoming a significant issue that seriously affects public health. Dietary intervention, serve as an essential constituent of lifestyle management, plays a vital role in the prevention and treatment of these diseases. This article reviews the research progress of low-purine diet, Mediterranean diet, and Dietary approaches to stop hypertension (DASH) diet in hyperuricemia and gout. Researches have indicated that the low-purine diet, as a traditional intervention strategy, can effectively reduce purine load, rapidly lower blood uric acid, and improve metabolic indicators; the MD can significantly decrease serum uric acid and reduce gout risk through improving insulin resistance, anti-inflammation, and promoting uric acid excretion; the DASH diet, while controlling blood pressure, reduces uric acid by increasing mineral intake and improving renal uric acid excretion. Although existing evidence indicates that all three dietary patterns have certain effects, the research still has limitations such as insufficient sample size, short follow-up time, and insufficient population specificity. Future study should carry on large-scale, multi-center clinical tests and combine multi-omics technologies to further clarify the mechanisms of dietary patterns on uric acid metabolism, in order to provide more reliable evidence for precise dietary intervention in hyperuricemia and gout.

Keywords: Hyperuricemia/gout; Low purine diet; Mediterranean diet; DASH diet.

1. Introduction

Hyperuricemia (HUA) and gout are common metabolic disorders that have been on the upward trend globally in recent years [1]. In 2020, the age-standardized prevalence of gout worldwide was 659.3 per 100,000 people, an increase of 22.5% compared to 1990. Gout is an inflammatory joint disease result from the deposition of urate vitrellas, with persistently elevated blood uric acid levels as its core patho-

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logical basis. Epidemiological data show that hyperuricemia is not only a necessary condition for the occurrence of gout but is also closely related to obesity, type 2 diabetes, cardiovascular diseases, and chronic kidney disease, posing a serious encumbrance on public health [2]. The occurrence of hyperuricemia and gout is mainly related to purine metabolism disorders and impaired uric acid excretion. Long-term hyperuricemia can lead to recurrent arthritis, accompanied by kidney damage and cardiovascular complications. Clinically, although drug treatments (such as allopurinol and febuxostat) can effectively lower uric acid, long-term reliance on drugs often comes with adverse reactions and low patient compliance. Therefore, lifestyle interventions, especially dietary regulation, have become important means for disease prevention and management.

Existing studies have shown that different dietary patterns have different influences on blood uric acid levels and the hazard of arthrolithiasis. For example, a low-purine diet is a traditionally recommended management strategy that can effectively reduce the intake of exogenous purines; the MD, have a large content of slumps, veggies, whole grains, and unsaturated fatty acids, has been certificated to have anti-inflammatory and metabolic syndrome-improving effects; while the DASH diet (Dietary Approaches to Stop Hypertension), in addition to lowering blood pressure, also shows positive effects on uric acid metabolism [3]. However, there is currently no systematic review of the relationship between different diets and hyperuricemia. Based on this, this article will review the research progress of low-purine diet, the MD, and DASH diet in the prevention and healing of hyperuricemia and gout, with the aim of providing references for clinical intervention and lifestyle management.

2. The Effect of Low Purine Diet on Hyperuricemia/Gout

Low purine diet is a classic dietary intervention model characterized by strict restriction of high purine foods intake, for instance animal organs, some seafood, red meat, and beer, while moderately increasing low purine foods for instance dairy, eggs, grains, vegetables, and greens to reduce uric acid production and deposition. This dietary pattern first proposed for nutritional treatment of arthrolithiasis patients, aiming to reduce serum uric acid through dietary control, prevent acute attacks and related complications. Since the 20th century, a low purine diet has gradually become an important component of hyperuricemia and gout management, and has been proven in clinical studies to effectively reduce serum uric acid and lower the risk of impatient disposition gout attacks [4]. At present, multiple evidence-based studies support the role of low purine diet in the prevention and treatment of gout, making it an internationally recognized basic dietary intervention measure [5].

The relationship between low purine diet patterns and hyperuricemia and gout, there is some research testimony including systematic reviews, prospective cohort studies, and clinical intervention trials. A systematic review summary shows that interventions with different dietary patterns generally have small to moderate effects on reducing serum uric acid, with a SUA range of approximately -0.3 to -2.9 mg/dL; In a comparative trial involving 98 gout patients, the febuxostat+low purine diet group was compared with the allopurinol+low purine diet group for a period of 6 months. The results indicated that the serum uric acid level in the febuxostat+LPD group was remarkably lower than that in the allopurinol+LPD group (about 162.39 μ mol/L vs. 198.32 μ mol/L, $p<0.001$), and the levels of inflammatory factors and joint pain were significantly improved after treatment, with a lower incidence of adverse reactions match the control group; The original intervention studies also support a significant short-term reduction in uric acid levels: another prospective cohort study involving 626 gout patients (average age 41.2 years, male 98%) showed that implementing a two-week low purine diet resulted in a significant decrease in serum uric acid from an average of 576.4 μ mol/L to 514.0μ mol/L ($p<0.001$) [3]. The decrease in different pathological types is in the order of „overproduction type“ (-88.8 μ mol/L)>“excretion disorder type“ (-57.3 μmol/L) [3]. In addition, this dietary pattern is accompanied by blood pressure BMI, Significant improvement in indicators for instance blood lipids, liver and kidney function [3]. Although research has not yet clearly indicated the impact of this diet on the frequency of acute gout attacks or changes in nodules, its effect on rapidly reducing serum uric acid and improving metabolic parameters has provided strong support for the overall management of gout.

The improvement of hyperuricemia and gout by a low purine diet pattern may be related to its direct reduction of purine load in the body and decrease in uric acid production. Specifically, reducing the intake of animal derived high purine foods can lower the supply of purine substrates, decrease the metabolic conversion of hypoxanthine/xanthine to uric acid, thereby lowering serum uric acid concentration and reducing the risk of urate crystal formation; It is also possible to inhibit fructose induced rapid ATP depletion and purine nucleotide metabolism hyperactivity by limiting the intake of fructose and sugary drinks, ultimately reducing the short-term uric acid production rate and alleviating the high uric acid burden

caused by causal sugars; In addition, a low purine diet promotes the intake of alkaline foods, thereby improving urine pH, increasing urate solubility, and enhancing renal uric acid excretion, ultimately reducing urate crystal deposition and inflammatory reactions. In summary, a low purine diet pattern can lower blood uric acid and reduce the risk of gout attacks through multiple metabolic and excretory pathways.

3. The Effect of Mediterranean Diet Pattern on Hyperuricemia/Gout

The Mediterranean diet is a typical healthy eating pattern, characterized by a large amount of greens, vegetables, whole grains, beans, and nuts as the basis, combined with olive oil as the main source of fat, and moderate intake of fish, poultry, and dairy products, while reducing the proportion of red meat and processed foods, and including moderate amounts of red wine in some populations. Numerous epidemiological studies showed this dietary pattern can reduce the risk of cardiovascular disease, improvement of metabolic syndrome, and decreased inflammation. Randomized controlled trials and systematic reviews further confirm that the MD can effectively improve blood lipid, blood glucose control, and weight management, and has potential benefits in delaying cognitive decline [6]. Therefore, the MD is not only a healthy eating pattern, but also gradually becoming an important basis for chronic disease prevention and healthy lifestyle promotion.

The MD also received much attention in the fields of hyperuricemia and gout in recent years. In a small sample pilot intervention study, half of the 12 hyperuricemia patients who participated in the test completed the MD intervention. The initial average serum uric acid was 9.12mg/dL, which decreased by 20% in the first month to 6.92mg/dL. The mean values after three months and six months of follow-up were 6.32, 6.10, and 6.40mg/dL, respectively; At the same time, the average BMI of participants before the trial was 31.46, and after six months of intervention, the average BMI decreased to 29.03, indicating a rapid and sustained uric acid lowering effect and improvement in overweight and obesity [7].

In addition, the Ikaria Geriatric Study showed that among 538 participants with an average age of 75 (281 female participants and 257 male participants), for every point increase in the MedDietScore, serum uric acid decreased by an average of 1.48mg/dL ($p<0.001$), and this correlation remained significant in males ($p=0.009$) [8]. The ATTICA cohort study further found that among 2380 male and female participants without cardiovascular or kidney disease, those who followed a high-altitude MD had a significantly reduced likelihood of developing hyperuricemia (UA>7.0mg/dL (male) or>6.0mg/dL (female)). The highest quartile of MedDietScore showed a 70% reduction in disease incidence compared to the lowest quartile (OR=0.30, 95% CI 0.11-0.82), and this reduction was significant in females, overweight individuals, and individuals with normal glucose metabolism [9].

At the same time, research found the improvement of hyperuricemia and gout in the MD may be due to the high fiber fruits, vegetables, and whole grains in the MD, which can improve insulin resistance and promote the excretion of uric acid by the kidneys, thereby reducing serum uric acid; The reduction in intake of both red meat and purine foods leads to a decrease in exogenous purine load and a decrease in uric acid production; In addition, polyphenols and unsaturated fatty acids found in olive oil, nuts, and deep-sea fish can reduce the risk of acute gout attacks by inhibiting oxidative stress and inflammatory responses, alleviating urate induced joint and soft tissue damage.

4. The Effect of Dash Diet Pattern on Hyperuricemia/Gout

The Dietary Approaches to Stop Hypertension(DASH) Diet, is a widely used healthy eating pattern that emphasizes high intake of greens, fruits, whole grains, low-fat dairy products, and lean meat, while limiting sodium, red meat, sugary drinks, and high saturated fatty acid foods [10]. This dietary pattern was first proposed by the National Heart, Lung, and Blood Institute (NHLBI) in the 1990s for the prevention and control of hypertension. The DASH diet is highly valued for its significant effects in lowering blood pressure, improving blood lipids and blood sugar levels, and is gradually being applied in the management of metabolic diseases.

In recent years, the DASH dietary pattern showed to have potential benefits in serum uric acid control. A randomized controlled study (DASH Sodium trial) was conducted 412 adult participants with an average age of 48 were randomly assigned to receive either DASH or a typical American control diet. The results showed that compared to a model American eating, the DASH diet significantly reduced overall serum uric acid by approximately 0.25-0.35mg/dL (95% CI -0.65 to -0.05, P=0.02)[11]. Further stratified analysis of the study revealed that among subjects (n=103) with baseline serum uric acid levels ≥ 6mg/dL, the effect was more significant: a continuous DASH diet for 30 days lead to an average decrease of approximately 0.8mg/dL in serum uric acid, reaching approximately 1.0mg/dL after 90 days, and over half of the patients (54%) had serum

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uric acid below 6mg/dL [12]. In addition, studies showed the DASH diet has a stronger uric acid lowering effect under low/moderate sodium intake backgrounds (low sodium group -0.53mg/dL; The moderate sodium group (-0.56mg/dL) showed that sodium intake may regulate the effect of diet on uric acid metabolism [13].

The regulatory mechanism of DASH diet on hyperuricemia and gout may emphasize the intake of high fruits and greens, whole grains, and low-fat dairy products, which can improve the alkaline environment of urine and increase uric acid solubility by increasing the intake of minerals for instance potassium, magnesium, and calcium, thereby promoting renal uric acid excretion and reducing serum uric acid concentration; At the same time, the DASH dietary pattern reduces the proportion of total fat and saturated fat, and the diet is rich in dietary fiber and phytochemicals, which can improve insulin sensitivity and energy metabolism, reduce renal tubular reabsorption of uric acid, and indirectly lower serum uric acid; In addition, the antioxidant nutrients (vitamin C, polyphenols) and other substances rich in this diet can diminish the risk of urathritis seizure by inhibiting oxidative stress and inflammatory signaling pathways, reducing the inflammatory response induced by monosodium urate crystals.

5. Limitations of Different Dietary Patterns

Although existing research suggests that multiple dietary patterns have potential benefits in reducing serum uric acid also decreasing the risk of gout attacks, there are still several limitations: firstly, there is significant heterogeneity in the study design. There are significant differences in dietary intervention content, purine restriction degree, intervention duration, and outcome indicators among different studies, leading to a lack of comparability among the results. For example, some trials only observe for a few weeks or months, making it difficult to evaluate long-term compliance and sustained effects; Secondly, there are issues with the small sample capacity and limited overallthe characteristics in the study. At present, most randomized controlled trials and cohort studies have limited sample sizes and are mostly concentrated in Western populations, lacking extensive validation for Asian populations or special populations (such as obese patients with metabolic syndrome), which reduces the extrapolation of results; In addition, the mechanisms of action of these dietary patterns in hyperuricemia and gout have not been fully elucidated. At present, the understanding of how diet affects diseases through pathways for instance purine metabolism, renal excretion, energy metabolism, and inflammatory response is still in the speculative stage, and there is still a lack of large-scale, multicenter mechanistic experimental evidence.

6. Conclusion

Based on the various theoretical models and empirical cases discussed earlier, it is not difficult to conclude that the Mediterranean diet, low purine diet, and DASH diet have all shown positive effects on the prevention and treatment of hyperuricemia and gout to varying degrees. The MD has good prospects in reducing blood uric acid and decreasing the risk of gout through its anti-inflammatory and metabolic syndrome improving properties; As a classic intervention model, low purine diet can rapidly reduce serum uric acid and improve metabolic indicators, and remains an important cornerstone of dietary management for gout patients; The DASH diet, on the other hand, demonstrates potential advantages in reducing serum uric acid by improving renal excretion and antioxidant pathways while controlling blood pressure. These dietary patterns not only provide beneficial supplements for drug therapy, but also offer diverse choices for lifestyle interventions for patients.

However, there are certain limitations to the current evidence, including insufficient sample size, short follow-up periods, significant differences in dietary compliance, and insufficient mechanism research. Therefore, the investigate in the future should lay particular emphasis on promoting large-scale, multicenter randomized controlled trials, combined with multidisciplinary approachesfor instance metabolomics and gut microbiome, to deeply reveal the mechanism of dietary patterns on uric acid metabolism and inflammatory response. At the same time, validation studies should be strengthened in Asian and other different ethnic populations to enhance the extrapolation and clinical application value of the results. In addition, exploring individualized dietary interventions for instance developing precise dietary plans based on genotype, metabolic status, and comorbidities is also expected to become an important direction for the prevention and treatment of hyperuricemia and gout in the future.

In summary, dietary intervention as a safe, economical, and sustainable lifestyle management tool will exert an increasingly important effect in the prevention and control of hyperuricemia and gout.

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