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Update on Importance of Diet in Gout

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ABSTRACT

Gout is an inflammatory arthritis caused by deposition of monosodium urate crystals within synovial joints. Although it is most well-known for its arthritis, gout has an intimate relationship with many other cardiovascular and metabolic conditions. Current recommendations support aggressive medical therapy to treat gout, whereas dietary counseling has become less emphasized. This article argues for the absolute importance of dietary counseling in gout and proves why this counseling may impact the long term well-being of a patient with gout.

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Gout is an inflammatory arthritis caused by deposition of monosodium urate crystals within synovial joints as a result of elevated serum uric acid (SUA) levels.[1] The classic symptoms described are recurrent "attacks" of severe pain, swelling, redness, and warmth in one or a few joints; in some cases it can become chronic and polyarticular.[2]

In the United States the estimated prevalence of gout is 8 million individuals, which is an increase of approximately 1.2% over the last 20 years.[3-5] When comparing 2 incidence cohorts from 1977-1978 and 1995-1996 in Minnesota, the incidence of primary gout was shown to have increased from 42 to 62.3 per 100,000 ($P = .1$) over the 20-year period.[6] Other studies have shown this trend to be worldwide. In New Zealand, where gout is especially common, the prevalence is estimated at 2.69% and rose as high as 25% in elderly men.[7]

Because of new pharmacotheraputics targeting hyperuricemia, healthcare providers often start medical therapy sooner and give dietary counseling less emphasis.[8] With this approach comes the inherent risk of drug toxicity, interactions, and polypharmacy in patients who often have multiple comorbidities. However, if the approach to gout treatment included dietary therapy and lifestyle modification, it could lower uric acid levels as well as potentially mitigate the long-term consequences of the metabolic syndrome that often coexist with gout.[9,10]

GOUT AND METABOLIC SYNDROME

It has been well described that gout affects those who tend to be overindulgent; hence the name "The Disease of Kings." Although gout is not formally included in the metabolic syndrome definition, they share common conditions, such as obesity, dyslipidemia, insulin resistance, and hypertension. The prevalence of metabolic syndrome is 62.8% in patients with gout, compared with 25.4% in non-gout patients.[11] Whereas 3.4% of people with weight below the 20th percentile are hyperuricemic, 11.4% of those above the 80th percentile have elevated serum urate.[10] Hypertension was shown to be directly related to serum urate levels in mice treated with uricase inhibitors; their blood pressure rose proportionally to their uric acid.[12] Several recent small clinical trials have demonstrated that SUA-lowering agents, such as allopurinol and probenecid, can reduce blood pressure in adolescents.[13,14] Hyperlipidemia has been found in 25%-60% of gout patients, whereas hypertriglyceridemia was seen in 53.7% of gout patients versus 35.3% of non-gout patients.[9] Insulin resistance has been found in 48.4%-76% of patients with gout, with the observed relative risk for incident type 2 diabetes mellitus in gout patients being 1.34 (95% confidence interval [CI] 1.09-1.64) compared with those without gout.[9,10,15] The prevalence of coronary heart disease is estimated at 25% of gout patients in the United Kingdom and 18% in the United States.[9] When compared

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with men without gout or coronary heart disease, men with gout had a relative risk of 1.28 (95% CI 1.15-1.41) for total mortality and 1.55 (95% CI 1.24-1.93) for fatal coronary heart disease.[16] In the Multiple Risk Factor Intervention Trial (MRFIT), gout patients had an increased risk of myocardial infarction of 26% and a 35% risk of coronary heart disease.[9] Although gout is sometimes thought of as just an inflammatory arthritis, it is not difficult to illustrate the relationship with other cardiovascular and metabolic conditions and long-term poor outcomes.

CLINICAL SIGNIFICANCE

- Gout is a prevalent disease.
- Gout has strong associations with many comorbid conditions.
- Diet is the common thread between these conditions.
- Dietary modifications can impact hyperuricemia and gout flares, as well as metabolic syndrome, hypertension, and coronary artery disease.
- Certain foods and supplementation may improve hyperuricemia, gout flare control, and prevention.

Dietary measures likely play a greater role than urate-lowering therapy in the long-term management of metabolic syndrome commonly associated with gout. A self-reported incident gout trial found that men with a body mass index (BMI) over 27.5 were 16 times more likely to report gout flares than men with a BMI <20 kg/m^2.[17] Compared with men with a BMI of 21-22.9 kg/m^2, the relative risk of gout for a BMI of 25-29.9 kg/m^2 was 1.95 (95% CI 1.44-2.65), BMI of 30-34.9 kg/m^2 was 2.33 (95% CI 1.62-3.36), and a BMI of ≥35 kg/m^2 was 2.97 (95% CI 1.73-5.1).[18] In a small cohort of obese men with gout who were started on a moderate calorie and carbohydrate restriction diet for 16 weeks, there was an average weight loss of 5.4 kg, an average decrease in monthly gout flares from 2.1 to 0.7 (P = .002), and a decrease in serum urate of 0.57 mg/dL to 0.47 mg/dL (P = .001). Of the 12 men who initially had a high serum urate, 7 became normalized.[19] In the MRFIT trial, when compared with no weight change, the odds ratio for reaching normal urate with a loss of 1-4.9 kg was 1.43 (95% CI 1.33-1.54), 5-9.9 kg was 2.17 (95% CI 1.95-2.4), and ≥10 kg was 3.9 (95% CI 3.31-4.61). The decrease in serum urate levels for each bracket of weight loss was −0.12, −0.31, and −0.62 mg/dL, respectively.[20] Therefore, obesity is associated with gouty flares and hyperuricemia, and weight loss is one of the most important modifiable risk factors for gout.

SINGLE FOOD/SUPPLEMENTS EFFECTS ON HYPERURICEMIA AND GOUT

The National Health and Nutrition Examination Survey studies were designed to assess the health and nutritional status of citizens in the United States. Questionnaires, examinations, vital signs, and laboratory data were collected over time, to assess risk factors for certain diseases. Much of the data on diet and gout come from these studies. For each of the following foods for which National Health and Nutrition Examination Survey data are used there will be a description of certain associations found, but given the design of the studies and the large number of variables, there must be caution in assuming true causation.

Alcohol

The risk of hyperuricemia and gout differ both with amount and type of alcohol ingested. National Health and Nutrition Examination Survey data from men show that when compared with no alcohol ingestion, beer was found to increase serum urate 0.46 mg/dL per drink per day (95% CI 0.32-0.6) and liquor 0.29 mg/dL per drink per day (95% CI 0.14-0.45) (P <.001). Wine was not found to be associated with increased urate (P <.001). Body mass index was very similar among beer, liquor, and wine drinkers in this study. In 2 different multivariate analyses, after adjusting for BMI, the affect from each type of alcohol on serum urate remained.[21] Cross-sectional data show similar trends in women: each serving of beer per week increased serum urate by 0.03 mg/dL.[22] A prospective cohort study of men followed for over 12 years showed that compared with nondrinkers, the relative risk of incident gout in drinkers was 1.32 (95% CI 0.99-1.75) for 10-14.9 g/d, 1.49 (95% CI 1.14-1.94) for 15-29.9 g/d, 1.96 (95% CI 0.48-2.6) for 30-49.9 g/d, and 2.53 (95% CI 1.73-3.7) for at ≥50 g/d. The relative risk was 1.49 (95% CI 1.32-1.7) per 12-oz beer per day, 1.15 (95% CI 1.04-1.28) per shot of liquor per day, and was found to be unassociated with wine intake, 1.04 (95% CI 0.88-1.22).[23] There have been many proposed mechanisms to explain how alcohol affects urate. An early study proposed that this was from increased adenosine triphosphate consumption, causing eventual increased uric acid production.[24] Serum lactate was also recorded here and found to be elevated, which although since unproven, was postulated to decrease uric acid excretion.[24,25] Others have proposed that increased purine loads in beer cause increased uric acid production.[26] In a study of alcoholic versus nonalcoholic beer, both were found to increase serum urate levels, 6.5% versus 4.4% respectively, arguing that the ingestion of the purine load alone can increase uric acid levels.[27]

Purine-Rich Foods

Purine-containing foods (such as meats, organ meat, seafood, legumes, yeast, mushrooms, and gravies) have been the target of many early gout diets, mainly on the basis of the concept that the biochemical degradation end product of purines is urate. More recent studies have found that this is not necessarily true. National Health and Nutrition