How effective is prophylactic therapy for gout in people with prior attacks?

EVIDENCE-BASED ANSWER

Colchicine (strength of recommendation [SOR]: **B**, based on 1 double-blind crossover study), allopurinol (SOR: **B**, based on 2 cohort studies), and weight loss (SOR: **B**, based on 1 small cohort study) have been shown to reduce symptomatic recurrences of gout, although the data to support their use is limited. Some evidence suggests that despite their serum uric acid–lowering effects, uricosurics (such as probenecid) fail to reduce gout attacks (SOR: **B**, based on 2 cohort studies). We were unable to find any double-blind, placebo-controlled long-term outcome studies addressing this problem.

EVIDENCE SUMMARY

The majority of gout sufferers are uric acid undersecretors rather than overproducers; however, many patients will have a combination of these 2 processes, as well as caloric or purine overindulgence. Efforts to limit the frequency and intensity of gout attacks have focused on reducing the uric acid load or reducing the inflammatory response to intra-articular crystal deposition. Pharmacologic therapies include 1) uricosurics, such as probenecid, sulfinpyrazone and benzbromarone (used mostly in Europe), which increase the renal clearance of uric acid, 2) xanthine oxidase inhibitors such as allopurinol, which limit the formation of uric acid to yield a more water soluble chemical, and 3) anti-inflammatory medications, including nonsteroidal anti-inflammatory drugs (NSAIDs) and colchicine. Obesity and insulin resistance are associated with elevated uric acid, suggesting that weight loss may also help reduce episodes of gout.

A double-blinded crossover study of 38 veteran men with recurrent gout found that the addition of daily colchicine to uricosurics reduced the frequency of attacks by nearly two thirds in 6 months of follow-up.[1] A cohort study of 208 men with confirmed gout who used either daily colchicine alone or colchicine with uricosurics for 2 to 10 years found marked improvements in attack frequency in both groups, yet there was no difference between the intervention groups.[2] An additional study followed 734 patients (including some of the subjects in the first cohort study) and reported similar outcomes.[3]

Allopurinol was studied in 46 patients using prophylactic colchicine with an average follow-up of 12 months.[4] Attack rates were unchanged for the first several weeks followed by a decline in the attack rate and a regression of tophi. When allopurinol was added to uricosurics in 48 patients, tophi were reduced.[5]

An average weight loss of 7.7 kg had a beneficial effect on serum uric acid levels and gout attack rates in 13 nondiabetic men, who were placed on a carefully controlled 1600-calorie diet with 40% of calories from complex carbohydrates.[6]

In a small study, the addition of uricosurics did not reduce the gout attack rate in 14 patients with nontophaceous gout.[7] Patients were followed over 12 to 15 months in a crossover study of colchicine and placebo versus colchicine and sulfinpyrazone. Although this study had limited power, a larger cohort study had similar findings over a longer follow-up period.[3]

We were unable to find any applicable studies of daily NSAID use, dietary purine control, or alcohol reduction for the secondary prevention of gout. A prospective study of primary gout involving 47,150 men followed over 12 years noted a relative risk (RR) of gout 1.41 (95% confidence interval [CI], 1.07–1.86) in the highest quintile of meat eaters, a RR of 1.51 (95% CI, 1.17–1.95) in the highest quintile of seafood eaters, and an inverse relationship of dairy intake with gout risk.[8] Thiazide diuretics appear to increase the likelihood of a gout diag-

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nosis and if used, could be discontinued, although no studies have investigated this intervention. Most of the gout studies were performed in the 1960s using simple cohort designs and limited statistical analysis; some used combinations of medications and variable dosing. Only allopurinol appears effective in resorbing tophi[5] and may have greater utility for patients with severe tophaceous gout, in those intolerant to uricosurics, in gross overproduction of uric acid, for patients with uric acid stones, or for those with renal impairment.

RECOMMENDATIONS FROM OTHERS

An expert panel, recruited by the Agency for Healthcare Research and Quality, recently published a summary combining evidence and expert opinion, which suggested that colchicine is a good prophylactic therapy and that uric acid lowering drugs (allopurinol, probenecid, and sulfinpyrazone) are effective in decreasing attack frequency in those with more than 2 attacks per year.[9] Weight loss and alcohol reduction were also encouraged. A Cochrane review of this topic is scheduled for completion in 2004.

Vincent J. WinklerPrins, MD, Arlene M. Weismantel, MILS, Michigan State University, East Lansing

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CLINICAL COMMENTARY

Prophylactic therapy is recommended for frequent attacks

Long-term therapy is recommended when frequent gouty attacks occur. Care is warranted in the use of colchicine with erythromycin, simvastatin, and cyclosporine, since these drugs modify the excretion of colchicine, which may lead to toxic doses.[10] Uric acid–lowering agents, such as allopurinol and probenecid, should be avoided in acute attacks of gout, due to potential worsening of inflammation.

Nonadherence with long-term prophylactic therapy for gout can lead to acute attacks, but patients who adhere to prophylactic therapy can still experience occasional acute breakthroughs of gout. The Cochrane review in progress may shed more insight into the prevention of acute gouty inflammation..

Thuy Hanh Trinh, MD, Baylor College of Medicine, Houston, Tex

Does tight control of blood glucose in pregnant women with diabetes improve neonatal outcomes?

EVIDENCE-BASED ANSWER

In pregnant women with preexisting type 1 diabetes mellitus, maintaining near-normal blood glucose levels decreases the rate of major congenital anomalies (defined as those causing death or a serious handicap necessitating surgical correction or medical treatment). Prolonged preconception control of blood sugar to near-