TREATMENT

Management of Acute Gouty Attack

The goal of management is to quickly control the inflammation and pain. Affected joints should be rested. Application of ice to the joint is usually helpful in reducing symptoms, but it is rarely sufficient to adequately control symptoms.

*Nonsteroidal anti-inflammatory drug*s (NSAIDs) including ibuprofen, naproxen, indomethacin, and diclofenac are typically used, and all seem to be equally effective. Full doses of NSAIDs should be initiated immediately, and a treatment duration of 7 to 10 days may be necessary for complete resolution of symptoms. NSAIDs are inappropriate in patients with peptic ulcer disease, inflammatory bowel disease, or renal insufficiency, and they must be used with caution in patients who are at risk for cardiovascular events.

Oral colchicine can be effective if it is used early in an acute attack (i.e., within the first 24 to 48 hours). A commonly prescribed dose is 1.2 mg, followed by 0.6 mg 4 hours later for the first day, followed by dose tapering until the attack is resolved. The drug should be stopped if nausea or loose stool occurs. Use of intravenous colchicine is discouraged because of the unacceptable risk of bone marrow suppression. Intraarticular corticosteroid injection is a very effective therapy for patients with monoarticular or oligoarticular disease in whom other systemic therapies need to be avoided. Enteral or parenteral glucocorticosteroids are effective in patients with renal insufficiency, intolerance to NSAIDs or colchicine, or treatment resistance. This approach is usually reserved for polyarticular flares when intraarticular injection is not practical (i.e., too many involved joints). A common starting corticosteroid dose is prednisone, 30 to 50 mg daily.

Urate-lowering therapy (ULT) should *not* be interrupted during acute attacks. Patients with established disease should be encouraged to maintain a supply of their medication for acute attacks and to start it promptly at the onset of typical symptoms; this may shorten the duration of attacks.

Management of Intercritical and Chronic Gout

Urate-Lowering Therapy

The aim of chronic treatment is to prevent recurrent attacks and to minimize joint damage by depleting tophaceous deposits in joints and soft tissue. This is achieved by lowering the uric acid level to less than 6 mg/dL. A target serum uric acid concentration of less than 5 mg/dL should be considered in patients with chronic tophaceous gout because it can result in a faster, more effective reduction in tophus size and flare frequency. Indications for ULT in patients with gout include two or more attacks in a single year, recurrent nephrolithiasis, and presence of tophi or chronic gouty arthritis.

ULT agents are divided into three categories: those that decrease uric acid production (uricostatic), those that increase renal excretion (uricosuric), and those that metabolize uric acid (uricolytic). The optimal duration of ULT is not known, and lifelong therapy is usually recommended. ULT is typically started after resolution of an acute attack.

Uricostatic Therapy

Allopurinol and febuxostat are xanthine oxidase inhibitors that prevent urate formation. They are effective in both overproducers and undersecretors of uric acid.

Allopurinol remains the first-line and most commonly used ULT agent, particularly in patients with chronic renal insufficiency, uric acid stones, or uric acid overproduction. If renal function is normal, a starting dose of 100 mg daily is recommended because higher doses may increase the risk of allopurinol hypersensitivity, a potentially lethal complication. The risk of early flares may also be increased with higher doses. It is recommended that the allopurinol dose be titrated up by 100 mg increments every 2 to 5 weeks until the uric acid goal is reached. The maximal dose is 800 mg/day. Adverse events include rash (2%), hepatitis, vasculitis, eosinophilia, and bone-marrow suppression.

Allopurinol hypersensitivity reaction can be fatal, and the risk may be higher with concomitant use of thiazides and in patients with penicillin allergy. Fever, severe exfoliative dermatitis, eosinophilia, and hepatic and renal failure can occur. If the uric acid goal is not achieved with allopurinol titration, or if side effects occur, then febuxostat may be used.

If the target uric acid level is not achieved with monotherapy, combination therapy with a uricosuric agent and a xanthine oxidase inhibitor may be considered.

Uricosuric Therapy

In the United States, probenecid is the only available uricosuric agent. It may be used as a first-line ULT in uric acid undersecretors (<600 mg in a 24-hour urine collection), but it is ineffective in patients with renal insufficiency (glomerular filtration rate <50 mL/minute) and is contraindicated in patients with nephrolithiasis. Patients should maintain high urine volume by drinking at least 1.5 L of fluid daily.

Uricolytic Therapy

Pegloticase (pegylated recombinant uricase), administered intravenously every 2 weeks, is considered for patients whose gout is refractory to conventional ULT.

Rasburicase, another recombinant uricase, is used to prevent tumor lysis syndrome but has no role in the management of gout.

Non–Urate-Lowering Prophylactic Therapy

Anti-inflammatory prophylaxis using low-dose colchicine or NSAIDs is usually recommended in conjunction with ULT to decrease the risk of flares that often accompany initiation of ULT. Prophylactic treatment is usually continued for 6 months after the serum uric acid goal is achieved.

Lifestyle Modifications and Education

A patient newly diagnosed with gout should be evaluated for potentially modifiable risk factors and associated illnesses such as obesity, hypertension, and hyperlipidemia. Decreased consumption of high-purine foods (e.g., shellfish, liver, sweetbreads) and fructose-containing beverages, as well as reduced alcohol intake, should be recommended. Diuretics should be avoided if possible.