Patients should be advised on weight loss and alcohol intake in Gout management

The peak age for the first attack of gout is during the fifth decade.

Dr Fahim Khan discusses the history and epidemiology of Gout, and advises on how to manage the condition.

The first clinical description of a syndrome called podagra, a classic pattern of gout was in the 5th century B.C.

Gout is a metabolic disease related to abnormal uric acid metabolism. Overproduction or, more commonly, undersecretion of uric acid leads to the deposition of monosodium urate crystals in the joint and soft tissues.

The natural history of gout classically has three stages. Asymptomatic hyperuricemia usually exists for years before the initial acute attack. Acute intermittent gout then develops. Patients have acute attacks followed by symptom-free periods. The attacks become more frequent until chronic gouty arthritis ensues.

In these patients, the intercritical periods are no longer asymptomatic and joint pain persists. Tophi (uric acid deposits) are often seen in these patients.

Epidemiology. In the United States, approximately 12% of family members of gout patients are affected. Ninety percent of primary gout patients are men. The peak age for the first attack of gout is during the fifth decade.

Primary Gout. In primary gout, hyperuricemia results from a disorder of purine metabolism or from abnormal excretion of uric acid. Most patients with primary gout fall into an idiopathic category because no precise genetic or metabolic defect can be identified.

In approximately 1% of the primary gout group, specific enzyme defects have been found. Deficiency hof hypoxanthine guanine phosphoribosyltransferase (HGPRT) and increased activity of phosphoribosylpyrophosphate (PRPP) synthetase are the best-characterized forms.

Secondary gout constitutes about 10% of all gout cases. It can result from a variety of disorders that cause hyperuricemia as a result of overproduction or impaired excretion of uric acid. *(See Table 1).*

MANAGEMENT

Diagnostic workup

The diagnosis is based primarily on history, physical exam and the presence of urate crystals in joint fluid.

Patients with gout almost invariably have hyperuricemia, but uric acid levels may be normal during an attack. Attacks are also associated with an increased ESR and leukocyte count.

Aspiration of the joint is essential for diagnosis and reveals intracellular monosodium urate crystals. Monosodium urate crystals are needle-shaped and demonstrate negative birefringence with polarized microscopy.

Treatment

First and foremost, one should treat the acute attack, later, consider the need for treating hyperuricemia.

After the initial attack, educate patients about weight loss and decreasing alcohol intake. In addition, reevaluate the patient's drug regimen.

For example, if the patients is being treated with niacin for hypercholesterolemia or diuretics (especially thiazides) for HTN, make substitutions. Low-dose aspirin is commonly used in patients with coronary artery disease but may increase the risk of recurrent gout attacks.

Acute Gouty Attack

NSAIDs: Any NSAID can be used, but most studies use indomethacin.

Contraindications include peptic ulcer disease, chronic renal insufficiency, and drug allergy. Use aspirin with caution, as it impairs uric acid secretion.

Colchicine inhibits phagocytosis of urate crystals by neutrophils and also modifies chemotactic factors. It is most effective if started within the first 12-24 hours of the attack.

Oral dosing is limited by GI side effects, most predominately diarrhea with cramping that may be severe. Classically oral dosing is started with 1mg followed by 0.5mg q2h until the patient develops abdominal discomfort, diarrhea or reaches the 8mg/day maximal dose.

Most patients do not tolerate the classic dosing regimen due to severe GI side effects. Lower oral doses (e.g. 0.6mg bid) are a reasonable alternative. The patient should respond within 48 hours.

Corticosteroids: Intra-articular steroid injections are used frequently. They are a safe, local treatment for consideration in all patients once septic arthritis has been ruled out.

Oral Corticosteroid therapy is reserved for patients who have failed or have a contraindication to NSAIDs or colchicines or are experiencing a polyarticular attack. Prednisolone is started at 40 – 60mg PO qd and tapered over 7 days. A rebound attack may occur with tapering of corticosteroids. Rule out septic arthritis before initiating oral corticosteroid therapy.

ACTH/Corticotropin is a good option in patients who cannot tolerate colchicines or who have coexisting disease that precludes the use of colchicines or NSAIDs. Dose is 40 – 80 USP units SC or IM.

Analgesia: Acute attacks usually resolve spontaneously within 5-7 days. Patients with contraindications to the above therapies or complicating factorys (e.g. postop patients with NPO orders, renal failure and coagulopathy) may require opioid analgesics.

Ice applied to the affected joints for at least 30 minutes x 4 daily for 6 days can decrease pain and swelling with acute attacks.

Prophylactic therapy

The goal of prophylactic therapy is to prevent recurrent attacks. Give prophylactic therapy before the initiation of treatment to lower uric acid levels, as changes in uric acid levels (increases or decreases) may precipitate acute attacks.

The dose of colchicines is 0.6mg PO bid or 0.6mg PO daily if the patient has renal or hepatic disease. Possible side effects of long-term colchicine therapy include myositis and mixed peripheral neuropathy.

Daily indomethacin or other NSAIDs are useful. Use with caution in the elderly because of the risk of peptic ulcer disease and chronic renal insuffiency.

Treatment of Hyperuricemia

Consider treatment of hyperuricemia if the patient has tophaceous gout, gouty nephropathy, uric acid kidney stones, or repeated attacks (generally >three/year).

Do not start these agents during an acute attack, rather, start them 6-8 weeks after the attack subsides.

Continue therapy to lower uric acid levels indefinitely. A common mistake is stopping treatment when uric acid levels have normalized, which usually precipitates another attack.

Uricosurics. The goal is to lower urate to approximately 6.0 mg/dL (auto-analyzer measurement). Most commonly, these drugs are used in patients less than 50 years of age.

1. Indications ***(all must be present)***

(a) Normal urate excreter (<800mg/24 h)
(b) Normal renal function
(c) Absence of tophi
(d) No history of renal calculi.

2. Administration.

Prophylactic colchicine (0.6mg twice daily) should begin 3 days before therapy. Probenecid is the uricosuric drug of choice. The initial dosage is 250mg twice daily for 1 week. The dosage is increased to 500mg tow to three times daily depending on serum uric acid response. Adequate hydration must be maintained to prevent uric acid precipitation in renal tubules.

Allopurinol. The goal is to lower urate to approximately 6.0mg/dL.

1. Indications ***(only one need be present)***

(a) Hyperexcretion of urate (>800mg/24 h)
(b) History of renal calculi
(c) Tophi
(d) Renal insufficiency and gout
(e) There is another indication for lowering urate and uricosuric drugs are ineffective, not tolerated or contraindicated.
(f) Before cytotoxic therapy for neoplasis.
(g) Continued attacks of gout despite colchicine prophylaxis, uricosuric drugs or both. The severity of the gout attacks and the presence of radiographic joint damage are taken into consideration in the individual case.

3. Administration.

Prophylactic colchicine (0.6mg twice daily) can be started 3 days before initiation of allopurinol therapy. Some clinicians avoid oral colchicines in this setting and treat any flares of gout with NSAIDs or corticosteroids. Colchicine is appropriate for patients in whom prevention of gouty attacks during the initiation of the allopurinol therapy is felt to be especially important. When colchicine prophylaxis is used in this setting, it is generally continue for 6 months. The initial allopurinol dosage is 100mg daily, which is increased weekly until the maintenance dosage of 300mg daily is reached. Dosages as high as 600 to 800mg/d may be needed in a few patients to achieve clinical control. If the creatinine clearance is less than 20ml/min, the toxicity (skin rash, vasculitis, agranulocytosis) of allopurinol increases. The dosage of allopurinol is decreased according to decreased renal function. For a glomerular filtration rate of 20 to 30ml/min, the dose of allopurinol should be reduced to 100mg/d.

4. Allopurinol allergy.

Oxypurinol (an active metabolite of allopurinol) has been shown to be as effective as allopurinol and can be used (by special release from the manufacturer) in patients with allopurinol allergy. However, cross-reactive allerty has occurred in as may as 50% of cases. IV and oral desensitization regimens for allopurinol have been published.

Joint aspiration and intraarticular injection of corticosteroid preparations may be indicated for patients with persisting chronic synovitis.

Prevention of nephrolithiasis. In patients with renal stones, the following measures may be used.

Urine alkalinization. A urine pH greater than 6.0 can be achieved with one of the following:

Sodium or potassium citrate (Polycitra) (20ml four times daily). However, compliance with a regimen of dosing four times daily is difficult.

Acetazolamide (500mg at bedtime).

Large urine volume. The patient should be instructed to drink adequate fluids to produce at least 2L of urine daily.

Surgical therapy. Surgical removal of large tophi is indicated if they become infected or interfere with joint function.

References on request.

TABLE 1.

Overproduction of uric acid
Primary gout
Myeloproliferatvie disorders
Lymphoma
Hemoglobinopathies
Hemolytic anemia
Psoriasis
Cancer chemotherapy
Underexcretion of uric acid
Chronic renal failure
Lead nephropathy (saturnine gout)
Drugs; diuretics (except spironolactone), ethambutol, low-dose aspirin, cyclosporine
Lactic acidosis (alcoholism, pre-eclampsia)
Ketosis (diabetic, starvation)
Hyperparathyroidism
Hypertension
Overproduction and underexcretion
Glycogen storage disease, type 1
Mechanism unknown
Sarcoidosis
Obesity
Hypoparathyroidism
Paget's disease
Down syndrome

Dr Fahim Khan,
MBBS, MD, MRCP (UK)
BE, American Board of Rheumatology,
Consultant Rheumatologist
Aut Even Hospital, Kilkenny.
St Francis Private Hospital, Mullingar.