INVITED ARTICLE

GOUT

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ABSTRACT

Gout is a common disease in the primary health care setting. Diagnosis of primary gout is definite if urate crystals are present in synovial fluid or tophi. The colchicine therapeutic trial is a useful diagnostic aid but not specific. Secondary gout is associated with myeloproliferative disease. Non-steroidal anti-inflammatory agents or colchicine are the main stays of treatment in acute gouty arthritis. In the intercritical period, uricosuric agents or allopurinol can be used to control hyperuricaemia. Allopurinol is the treatment of choice in secondary gout. Asymptomatic hyperuricaemia is not an indication for therapy.

Keywords : *Hyperuricaemia, Sodium Urate, Tophus, Colchicine, Allopurinol*

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INTRODUCTION

Gout is an illness that is likely to be encountered fairly often in a primary health care setting. The joint symptoms have been well described as early as 1683 by Thomas Syndenham who was himself a victim of the disease. He tells of being awakened by "a severe pain in the great toe", which was "like a dislocation", "a violent stretching and tearing of the ligaments" so much so that "the night is spent in torture and sleeplessness"[1].

The prevalence of gouty arthritis as estimated from a long term population study in the United States was 1.5%[2]. The figure for males was 2.8% and for females it was 0.4%. Mean age of onset of arthritis was 47.7 for males and 54.1 for females. The big toe is affected in 76% of gouty patients, 50% have ankle or foot involvement and 32% have affected knees. Upper limb joints and multiple sites are less common[3]. Early attacks tend to subside spontaneously over three to ten days. Symptom-free intervals can vary from months to over ten years. Triggers for acute attacks include trauma, alcohol, drugs especially diuretics, surgical stress and acute medical illness. Urinary calculi were found in 15.4% of the patients with gouty arthritis[4-6].

The associations of gout are clinically important and should be looked for and treated. These include obesity, hypertension, a high alcohol intake, hyperlipidemia and cardiovascular disease.

In the management of gout, there are four important questions to answer. These are :

1) Is it gout?
2) What kind of gout?
3) How to treat?
4) What about asymptomatic hyperuricaemia?

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Is It Gout?

Diagnosis of gout is easier in some patients than others. The most specific (100% specific) test is the demonstration of characteristic sodium urate monohydrate crystals in the joint fluid. This is however only found in 85% of patients with acute gout. The presence of tophi proven to contain sodium urate crystals is 99% specific but only 30% sensitive.

Six or more of the following twelve criteria can also be used to diagnose gout :

1) Maximum inflammation developed within one day
2) More than one attack
3) Monoarticular arthritis
4) Redness over joints
5) First MTP pain or swelling
6) Unilateral first MTP involvement
7) Unilateral tarsal joint involvement
8) Suspected tophus
9) Hyperuricaemia
10) Asymmetrical swelling
11) Subcortical cysts, no erosions on X-rays
12) Negative organisms on culture

A patient can be classified as having acute gouty arthritis if he has urate crystals in the joint fluid and/or a proven tophus and/or six of the above twelve criteria[7].

The diagnostic value of the colchicine therapeutic trial was studied by Wallace et al[8]. 75% of patients with acute gout responded to colchicine. 5% of patients with other forms of arthritis also responded. The test is therefore useful but not infallible.

What Kind of Gout?

The classification of gout can be confusing. It may be more useful to consider clinical subsets as follows :

1) ***Primary Gout***
   - the typical patient
   - the young patient
   - the female patient
   - the elderly patient
2) ***Secondary Gout***

The typical gout patient is a middle-aged man, fond of good food and alcohol, has the clinical associations mentioned previously and classical big toe and lower limb arthritis.

Onset of gout before the age of thirty or gout in premenopausal women is a different clinical subset[9]. Over 50% with onset under the age of 25 and over 80% with onset between ages 12 and 19 have a positive family history of gout compared to 35% of the whole gouty population. The frequency of attacks is high and urolithiasis is more prominent. On the other hand, cardiovascular risk factors are less com-

mon. It is especially important to exclude other diagnoses in this group of patients by joint aspiration and crystal identification.

Gout in the elderly has a higher proportion of females compared to typical gout[9,10]. Polyarticular involvement, use of diuretics and renal insufficiency are more frequently encountered. There are fewer acute arthritic attacks and tophi. Drug side-effects are more likely to occur in this group of patients. Low dose colchicine is better tolerated than non-steroidal anti-inflammatory agents or allopurinol.

Secondary gout is associated with the myeloproliferative diseases[11] . This results from a high turnover of nucleic acid. Levels of serum uric acid tend to be very high, urinary excretion of uric acid is greater giving rise to more frequent urolithiasis and tophi are also more common. A positive family history is less common and male preponderance is also less than primary gout. Allopurinol is the treatment of choice.

How To Treat?

The management of gout varies with the phase of the disease. Management of the acute attack is best treated with a non-steroidal anti-inflammatory drug (NSAID) or colchicine. A short course of steroids may be required for severe cases of acute gout. Allopurinol should be avoided in this phase. Most NSAID's have been shown to be effective in acute gout. Colchicine is given orally in hourly doses of 0.5 mg or 0.6 mg until one of the following three conditions are met :

(a) significant improvement
(b) gastro-intestinal side effects
(c) a maximum dose of 6 mg over 24 hours has been given.

After a full course of 4 to 6 mg has been given, no more need be given for at least seven days as the excretion of colchicine is very slow. Intravenous colchicine is also effective.

Prophylactic colchicine has been shown to prevent recurrent attacks of acute arthritis. The lowest possible dose should be used.

Not every patient with an attack of acute gout needs to be started on an agent to lower serum uric acid. The interval between attacks can be very long. Uncontrolled hyperuricaemia does not lead to renal damage[12,13].

The indications for a uricosuric agent or allopurinol are as follows :

(a) visible tophi[14]
(b) major uric acid overproduction as in secondary gout
(c) frequent gouty attacks unresponsive to prophylactic colchicine or NSAID's
(d) recurrent uric acid renal calculi
(e) recurrent calcium oxalate renal calculi with hyperuricosuria.

Asymptomatic hyperuricaemia, acute attacks of gout, intercritical gout and non-tophaceous gout are NOT indications for starting therapy to lower serum uric acid.

Observing a low purine diet does help to lower serum uric acid although the reduction is rarely more than 2 mg/dl. Restriction on the following foods is advisable :

(a) Meats, poultry or other flesh; fish, sea food, sardines, herring, anchovies.
(b) Liver, kidney, heart, brain
(c) Yeast products, marmite, beer, alcohol
(d) Beans, peas, lentils, spinach, oatmeal, asparagus, cauliflower, mushroom.

Drugs that promote hyperuricaemia should be avoided. This includes diuretics, certain NSAID's, anti-tuberculous agents especially pyrazinamide and low-dose aspirin.

If starting an agent to lower serum uric acid is deemed necessary, the choice is between an uricosuric agent or allopurinol. An uricosuric agent should be the drug of choice as side effects are less commonly encountered compared with allopurinol and the majority of gout patients are underexcretors of uric acid. Allopurinol is preferred if the patient has renal insufficiency, urolithiasis, overexcretion of uric acid (600 mg/24 hours) or is receiving cytotoxic therapy for malignancy.

The uricosuric drugs most commonly used are probenecid and sulfinpyrazone. The dose of probenecid needed varies from 0.5 gm to 1.5 gm per day in divided doses. Therapy should be started with a small dose as gastric intolerance is fairly common. Probenecid decreases the excretion of many drugs including penicillin, ampicillin, indomethacin and dapsone. Aspirin blocks the uricosuric effect of both probenecid and sulfinpyrazone. Sulfinpyrazone is also started using a low dose. The effective dose varies between 100 mg to 800 mg per day. It has anti-platelet action. Side effects include gastric intolerance and rarely, marrow suppression.

Allopurinol is given once a day. The dose needed varies between 100 mg to 800 mg per day. It can potentiate the effect and toxicity of purine analogues such as 6-mercaptopurine and azathioprine. Drug reactions occur in 10.9% of patients. The hypersensitivity syndrome of fever, rash, hepato-renal injury and eosinophilia carries a mortality risk of 27.5%.

What About Asymptomatic Hyperuricaemia?

Asymptomatic hyperuricaemia is definitely NOT an indication for the use of allopurinol in view of the frequency of severe drug reactions. Early treatment of asymptomatic hyperuricaemia to reduce the risk of renal damage, stones or gouty arthritis is unproven and unjustified. Unnecessary treatment would do more harm than good[15,16].

There may be a role for treatment of patients who have a serum uric acid exceeding 13 mg/dl and urinary uric acid excretion greater than 1,100 mg over 24 hours. Universal agreement on this is lacking.

CONCLUSION

Treatment of gout is different from the management of asymptomatic hyperuricaemia. A normal serum uric acid does not exclude gout. A raised serum uric acid is not necessarily a cause for concern. The management of gout is often rewarding. Sound principles in diagnosis and treatment should be followed to ensure the best outcome for the patient.

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