

GOUTY ARTHRITIS: CURRENT TREATMENTS & NEW DEVELOPMENTS

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INTRODUCTION

Gouty arthritis, more commonly referred to as gout, is one of the best understood and most manageable rheumatic diseases (9). It is a painful condition caused by deposits of urate crystals in a joint, most commonly the big toe (1,2,5). Effective treatments are available for gout and others are being investigated all the time.

Uric acid is a by-product of purine metabolism in the body (1). Purines come from foods such as red meat, herring, asparagus and mushrooms. Uric acid has no biological function in humans (2). It is dissolved in the blood, passes into the kidneys, and excreted in the urine. An attack of gout occurs when the urate crystallizes into monosodium urate (MSU) crystals, and deposits in a joint, or joints, somewhere in the body. The build-up of the sharp, needle-like crystals causes pain and inflammation. Hyperuricemia is caused by increased production or decreased excretion of urate in the body (1,2,5,6). It is important to note that gout and hyperuricemia are not the same condition. As well, a person can have an attack of gout without the presence of hyperuricemia, and vice versa.

Gout is more prevalent in men than in women (1,6). It is usually first seen between the ages of 40 and 50 in men, and in post-menopausal women. Pre-menopausal women are less likely to develop gout because estrogen causes increased urate clearance.

Attacks of gout do not tend to have precipitating events (2). However, certain conditions can contribute to the development of gout, such as obesity, insulin resistance, hypertension, and hyperlipidemia (1,8). Crash dieting, a diet of rich foods and total parenteral nutrition may also contribute. Excessive alcohol consumption can predispose to gout (1,5,9). Excessive alcohol intake is defined as more than 2 drinks per day for men and more than one drink per day for women. It is important to note, however, that moderate wine consumption does not contribute to the development of gout.

Potential secondary causes of gout include infection, trauma and surgery, such as a renal allograft (2,5). Drugs that compete for renal excretion may also contribute. These include drugs such as loop and thiazide diuretics, low-dose Aspirin, and cyclosporine. Cyclosporine is particularly problematic in allograft patients; up to 80% of allograft patients on cyclosporine will develop hyperuricemia (9).

Some patients who experience an attack of gout will never have another one in their life (2,5). However, many patients experience recurrent attacks, so it is important to monitor patients and to provide both acute and possibly prophylactic treatment.

SIGNS & SYMPTOMS

An attack of gout usually occurs at night, suddenly and without warning (1,2,5). Pain is moderate at first and builds over several hours until it becomes almost unbearable. Initial attacks of gout are monoarticular (affecting only one joint) and are usually somewhere in the lower extremities. The most common manifestation of gout is called podagra (2). This is when the large joint of the big toe is affected. The affected joint becomes swollen, tender and red (1,2,5). This may also be accompanied by fever and chills. The pain is not sharp, but rather an intense pressure, like being squeezed in a vice.

Gout can also occur in the feet, ankles, knees, wrists and hands (1,2,5). The hips, shoulders and spine are rarely affected, likely due to these areas being of a slightly higher temperature that is not conducive to crystallization (8). Recurrent attacks of gout become polyarticular (affecting multiple joints) and will involve the ascending extremities (2). Prophylactic treatment of gout can be used in patients experiencing recurrent attacks.

DIAGNOSIS

Gout is suspected if a patient calls their physician complaining of joint pain and fever, though a joint fluid test is needed to make the official diagnosis (1,2). Synovial fluid is drawn from the inflamed joint and looked at under a microscope for the presence of MSU crystals. The crystals are long and needle-shaped. Serum urate levels are not usually used as an indicator of gout because, as has already been stated, hyperuricemia is not diagnostic of gout (6). An

increased serum urate level favours crystal formation, but even during an acute attack of gout the serum levels may appear normal.

TREATMENT

Acute

Episodes of gout are self-limiting and will resolve within 7 to 10 days without treatment (6). However, treatment can provide pain relief and speed the recovery process. The main reason for treatment failure is patient noncompliance, though this can be prevented with proper patient counselling. Treatment should be started as soon as possible after the diagnosis; the sooner the treatment is started, the quicker the response.

NSAIDs

Non-steroidal anti-inflammatories (NSAIDs) are used to relieve pain and inflammation, which is the immediate goal of anti-gout therapy (1,2). NSAIDs include indomethacin, ibuprofen, naproxen and diclofenac (4). NSAIDs are the drugs of choice for the treatment of gout because they are of long duration and have a better side effect profile than other anti-gout drugs, such as colchicine. These drugs are generally well-tolerated and the side effects are mild due to the short duration of therapy.

The choice of NSAID used depends on the patient (6). When improvement in symptoms begins to occur it is recommended to taper the dose to decrease the potential for gastrointestinal (GI) toxicity. NSAIDs are contraindicated for patients with heart failure, GI disease, renal insufficiency and those patients on anticoagulant therapy (4,5,6). Luckily there are other therapeutic options available for these patients.

Colchicine

Although NSAIDs are the preferred drugs for the treatment of acute gout, colchicine offers something NSAIDs do not: specificity. Colchicine is specific for gout (4). Patients who do not want to undergo a painful joint aspiration can be given colchicine. If the symptoms clear up, it is assumed that the patient had an attack of gout.

Colchicine is an antimetabolic that prevents MSU crystals from becoming deposited in joints (7). It also prevents phagocytosis of deposited MSU crystals, the process that contributes to inflammation. Colchicine is most effective within 10 to 12 hours of an attack, and will resolve an attack of gout within 2 to 3 days (4). The major flaw of colchicine is that it causes GI distress, resulting in nausea and vomiting or diarrhea (1,4). The appearance of these side effects coincides with improvement in joint symptoms. Patients are advised to take the drug until pain is relieved or adverse GI effects occur (2,3). Often GI distress occurs before pain relief, and patients are advised to stop taking the drug once they occur (6). Again, NSAIDs are generally preferred over colchicine its because of its adverse GI effects.

Corticosteroids

Corticosteroids such as prednisone can be used as a last resort for gout therapy, when neither NSAIDs nor colchicine can be used (1,9). As well, intra-articular steroids can be useful when medium to large joints are affected (9). Steroids are used to control pain and inflammation. Normally patients taking corticosteroids are given tapered doses when coming off of treatment (2,3). However, tapering is not usually necessary for gout patients because of the short duration of therapy.

Prophylaxis

Prophylactic treatment of gout involves decreasing uric acid production or increasing uric acid secretion (1,3,5). At the time of an acute attack, these drugs can actually worsen the problem; by rapidly decreasing serum urate concentration, urate stores will mobilize and prolong the attack (2). It is recommended to start prophylaxis 3 to 4 weeks after the resolution of an acute episode (2,6). Start therapy at a low dose and gradually increase over several weeks. It is also recommended to use colchicine prophylactically for one month, at a small daily dose of 0.5 to 0.6 milligrams (5).

Uricosurics

Uricosurics like probenecid and sulfinpyrazone increase renal excretion of uric acid by inhibiting tubular reabsorption in the kidneys (1,3). It is important to start at low doses because large amounts of uric acid passing through the kidneys will increase the risk of forming uric acid stones (2). The anti-hypertensive drug losartan has been shown to have a uricosuric effect, but this effect decreases drastically once the drug has reach steady-state (9). It can also worsen pre-existing renal impairment. Uricosuric drugs are contraindicated for patients with kidney stones and renal insufficiency (7,9). Those patients should use a drug that will function independently of kidney function.

Allopurinol

Allopurinol is a xanthine oxidase inhibitor and works to block the production of uric acid (1,2). Allopurinol works independently of renal function, so it is ideal for patients with renal insufficiency (5). Serum urate levels begin to fall within 1 to 2 days of beginning therapy, and will reach maximal suppression within 7 to 10 days.

Allopurinol is generally well-tolerated, but hypersensitivity reactions can be a problem (2,9). Rash is the most common adverse effect and patients are advised to discontinue taking the drug if a rash appears (3). There is an increased risk of hypersensitivity reactions in patients concurrently taking angiotensin converting enzyme inhibitors and thiazide diuretics.

Diet & Alcohol Intake

Dietary intervention, weight management and decreased alcohol consumption can reduce hyperuricemia in gout patients (9). Purine-restricted diets are not very palatable and rarely maintained, so researchers are looking into tailored, low-carbohydrate and calorie-restricted diets. It is recommended to increase protein and unsaturated fat intake, and to avoid crash diets and fasting (6,9). As was stated earlier, excessive alcohol consumption is associated with an increased risk of developing gout. Gout patients should be discouraged to avoid alcohol intake and to drink lots fluids (3,9). Dairy consumption has been associated with decreased risk

of gout, possibly due to a uricosuric effect of milk proteins (12). This association has not been entirely established yet and is still being researched.

Fenofibrate

Fenofibrate is emerging as a new possible prophylactic treatment for gout. The drug is normally used to treat hyperlipidemia by decreasing triglyceride levels and increasing HDL cholesterol levels (8). The drug has also been shown to lower serum urate levels. Long-term administration of fenofibrate has been associated with substantial and sustained decrease in serum urate. It has also been associated with a decrease in acute gout attacks.

One case report explains how a Type II diabetes mellitus patient, with a history of several gout attacks per year, has had no attacks since starting fenofibrate therapy (8). The patient has also had no need for prophylaxis. Another case report shows a patient with a history of gout responding well to fenofibrate therapy when other prophylactic treatments have failed.

Fenofibrate increases renal clearance of uric acid, an effect not seen with other fibrates (8). Although fenofibrate's urate-lowering effect is not as good as traditional uricosurics such as probenecid, researchers are suggesting it may be used in combination with other anti-gout drugs. Fenofibrate looks to be a promising adjunct to anti-gout therapy.

CONCLUSION

Gouty arthritis is a painful but readily treatable condition experienced by many adults. The prevalence of gout in Western countries is on the rise, most likely due to lifestyle choices. Hypertension, high alcohol intake, diuretic use (specifically, thiazides and loop diuretics) and obesity contribute both independently and additively to the development of gout in hyperuricemic patients (9). Prevalence is also rising in elderly patients, possibly due to high rates of diuretic use and the declining use of estrogen replacement therapy. This is problematic because traditional treatments for gout such as colchicine and NSAIDs have a higher risk of toxicity in elderly patients.

Research shows hyperuricemia to be a good predictor of ischemic cardiovascular diseases and poor outcomes related to these diseases (9). Although asymptomatic hyperuricemia is not an indication for therapy (3,9), researchers suggest that treating asymptomatic hyperuricemia may improve management of cardiovascular disease (9).

Though the treatment of gout has long been established, researchers are still finding potential new treatments, such as fenofibrate, and potential implications for treatment, such as outcomes in cardiovascular disease. Gout research remains an important endeavour.

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