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Consultant Pharmacist Continuing Education Series

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Gout

Gout is a form of arthritis that affects about one in fifteen Australians, with a higher prevalence in men and in Māori and Pacific Islander peoples. Gout hospitalisation rates have increased by 42% in the last decade. An estimated $230.8 million was spent on treatment and management of gout in 2020-21.

In gout, high levels of serum uric acid or hyperuricaemia results in precipitation of urate crystals in tissues and joints. This stimulates episodic and often severe inflammatory responses, resulting red, swollen painful joints. Typically, the big toe (first metatarsophalangeal joint) is affected. Ongoing urate deposition leads to progression of tophaceous deposits, further joint damage, and functional limitations.

Gout is associated with substantial pain, functional disability, significant comorbidity, and reduced quality of life, as well as social stigma. Many myths and misconceptions perpetuate with gout. It is often depicted as a disease of affluent individuals with profligate lifestyle associated with excessive alcohol intake and cause by certain foods. Gout should be viewed as a chronic metabolic disorder influenced by genetic predisposition.

Uric acid

The primary cause of gout is under-excretion of uric acid. Less commonly, a few conditions may cause over-production of uric acid and precipitate gout.

The plasma urate concentration is the single most important determinant of the risk of developing gout. Hyperuricaemia is defined as a serum uric acid greater than 0.36mmol/L in women and greater than 0.42mmol/L in men. The risk of developing gout increased at increasing serum urate levels.

Asymptomatic hyperuricaemia is common and is insufficient to diagnose gout. It is associated with an increased frequency of ischaemic heart disease, heart failure, atrial fibrillation, cerebrovascular accidents and cardiac deaths.

Changes in urate levels can result from acute alcohol ingestion, acute overindulgence in foods high in purines, rapid weight loss, dehydration, or trauma. Changes in the dosage of medications that raise or lower uric acid levels may also precipitate a gout attack.

Symptoms

Gout flares or attacks can be triggered by acute increases and decreases in urate levels that lead to production, exposure and shedding of crystals.

Gout symptoms typically develop rapidly with intensely painful swelling, usually a single joint. People complain of severe pain, swelling and tenderness that reaches its maximum within 6-12 hours, especially with overlying erythema and skin sensitivity.

An attack of a single joint usually resolves within a few days but may last for weeks. The skin around the area may peel as the attack subsides.

Management of gout

Management of gout includes several factors:

- Rapid symptom relief for acute attacks
- Life-long urate lowering therapy, using a treat-to-target approach
- Prophylaxis to prevent gout flares when starting urate-lowering therapy
- Address modifiable risk factors and optimise management of comorbidities
- Maintain healthy lifestyle and limit alcohol intake

Treatment

The two goals of treatment are to lower serum uric acid below the target value and treat acute flares and inflammation.

Acute gout treatment

An acute attack of gout should be treated at the earliest sign of symptoms to limit pain and inflammation, and possibly shorten the duration of the flare. Choice of medication primarily depends on comorbidities. These treatments do not reduce serum urate concentrations nor prevent progressive joint damage.

Treatment includes:

- NSAID
- Prednisone or prednisolone
- Colchicine

NSAIDs and intra-articular or oral corticosteroids (prednisone/prednisolone) are typically administered for 3 to 5 days or until symptoms subside. Concurrent proton pump inhibitor (PPI) may be used with NSAIDs for people with a risk of gastrointestinal adverse effects.

Low-dose colchicine (two 0.5mg tablets followed by one tablet 1 hour later) is effective when prescribed within 12 hours of onset of an acute gout flare, with a low incidence of gastrointestinal adverse effects. Higher dose have previously been recommended (2 tablets followed by 1 tablet every hour for 6 hours), but provide no additional clinical benefits, and often result in significant gastrointestinal toxicity.

Urate-lowering therapy should be continued during flares and may be commenced during a flare.

Chronic gout treatment

Chronic gout is treated with xanthine oxidase inhibitors (allopurinol and febuxostat), colchicine, NSAIDs and prednisone/prednisolone.

Allopurinol *(Zyloprim)* should be commenced at a dose of 50 mg orally, daily for the first month, then increased by 50 mg every 2 to 4 weeks depending on the patient's renal function and plasma urate levels. Lower starting doses are recommended in people with chronic kidney disease. The maintenance dose may vary from 300mg to 900mg daily. The dose of allopurinol should be increased until serum uric acid is less than 0.36mmol/L, or less than 0.03mmol/L if tophi are present. This is termed the treat-to-target approach.

Adverse effects occur in less than 1% of people treated with allopurinol. Drug-induced multi-organ hypersensitivity syndrome is a rare but life-threatening allergic reaction to allopurinol. Hypersensitivity reactions occur in the first 3 months of treatment and are often associated with high starting doses, especially in patients with renal impairment. Stopping allopurinol immediately on presentation of a rash and treating with corticosteroids usually improves symptoms. Genetic testing (HLA–B*5801) in selected populations can identify people at risk for allopurinol hypersensitivity syndrome.

Febuxostat *(Adenuric)* acts in the same way as allopurinol, as an inhibitor of xanthine oxidase. It is indicated on the PBS if a medical contraindication to allopurinol or documented history of allopurinol hypersensitivity syndrome or intolerance to allopurinol necessitating permanent treatment discontinuation. Unlike allopurinol, febuxostat treatment should not be started until an acute attack of gout has completely subsided.

Febuxostat is not recommended for people with pre-existing major cardiovascular disease. The incidence of rash with febuxostat is not significantly different from the incidence with allopurinol, but hypersensitivity syndrome may be less common.

Flare prophylaxis

Flare prophylaxis is recommended for all people when starting allopurinol. Prophylaxis should be continued for at least 6 months until the person reaches target uric acid levels and has no further attacks. Colchicine is recommended in a dose of 0.5mg daily. If colchicine is not appropriate, low dose NSAIDs or prednisolone may be considered.

Diet

It is a common misconception that gout is solely caused by lifestyle factors such as shellfish, red meat, alcohol and sugary drinks containing fructose. Current evidence suggests that avoidance of purine-rich foods has only a minimal effect and does not replace the need for urate-lowering therapy. Weight loss, daily activity and avoiding excessive alcohol intake should be encouraged in all patients with gout.

References
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Aust Prescr 2015;38(40):139-40.