
Time to Re-examine the Management of Gout

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Until recently, there had been very little change in our understanding of gout and in the treatment options available. Consequently, there may have been limited incentive for health-care professionals to learn more about this chronic condition or to question the methods they use to treat it.¹ There is, however, an evolving understanding of the underlying mechanisms behind the development of gout. This understanding may have a significant impact on the treatment modalities used to manage this common condition. Now is the time for clinicians to take another look at hyperuricemia and gout.

EPIDEMIOLOGY

Not all individuals with elevated serum uric acid (sUA) levels will develop the clinical disorder of gout, but despite that, gout is a relatively common condition in Canada and other Western countries, with a prevalence of approximately 1-3% of the overall population.^{2,3} In Canada, there are more than one million patients with a diagnosis of gout.³ The prevalence is considerably higher in males than females, particularly in younger adults; however, in the population older than 60 years, the inter-sex difference narrows considerably as a woman's risk of developing gout increases post-menopause.^{3,4}

Overall, the prevalence of gout appears to be increasing,⁵ attributable to the increase in associated metabolic risk factors in Western countries (*e.g.*, metabolic syndrome, obesity and hyperlipidemia),⁴ as well as genetic factors (family history).³ Our aging demographic is also expected to contribute to a rise in the prevalence of gout in Canada.⁴

PATHOPHYSIOLOGY

Gout is a metabolic disorder characterized by the deposition of monosodium urate (MSU) or uric acid crystals from hyperuricemia. The crystals provoke a potent inflammatory response,⁶ which leads to the acute symptoms and long-term progressive clinical manifestations of the disease—acute gouty arthritis, gouty arthropathy, chronic tophaceous gout, uric acid nephrolithiasis, and uric acid nephropathy.⁷ The inflammatory process involves the release of multiple cytokines (including interleukin-1 [IL-1], IL-6, and tumor necrosis factor [TNF], to name a few), which perpetuate inflammation in response to MSU crystals *in vitro*. Increased levels of IL-6, IL-8, and TNF occur in gouty tissues *in vivo*. Blockade of some of these cytokines has been shown to prevent MSU-induced inflammation in animal models.⁸

Gout attacks frequently recur. Approximately three-quarters of patients who suffer a gout attack will experience another within two years, and more than 60% will have a subsequent attack within one year.⁹ Only 7% will remain gout-free for more than 10 years.⁹

There are a number of potential precipitants for hyperuricemia and acute episodes of gout. These risk factors include advancing age, underlying chronic kidney disease, some medications, and possibly factors such as diet and alcohol.

Acute gout can have a substantially detrimental impact, with significant pain, inflammation and swelling interfering with quality of life.¹⁰ Over time, the inflammation can cause considerable joint destruction and renal damage.^{7,11,12}

MANAGEMENT

There are several goals in the management of gout: a) minimizing precipitants; b) treating acute episodes and associated pain; and c) lowering excess stores of uric acid to prevent the emergence of future flares and tissue damage.¹³

TREATING SYMPTOMS

The acute management of gout mainly involves the suppression of pain and reduction of inflammation, typically with nonsteroidal anti-inflammatory drugs (NSAIDs) (e.g., indomethacin 50 mg p.o. t.i.d., naproxen 500 mg p.o. b.i.d.). Other agents that may provide benefit for acute flares include colchicine (e.g., 0.6 mg p.o. b.i.d.-q.i.d.) and corticosteroids (either orally or as an intra-articular injection).

PREVENTION OF RECURRENT GOUT

The approach for prevention should include a combination of lifestyle modification, comorbid disease management, and eventually, pharmacologic therapy centred on anti-hyperuricemia in combination with prophylactic anti-inflammatory therapy, usually with low-dose NSAIDs or low-dose colchicine.

PHARMACOLOGIC ANTIHYPERURICEMIC THERAPY

Controlling sUA to levels at or below 360 µmol/L has been advocated.^{7,14,15} Pharmacologically, there are two ways to lower body uric acid stores: stimulating its elimination (with uricosuric agents such as probenecid) or reducing its formation (with a xanthine oxidase [XO] inhibitor such as allopurinol).¹⁴ The latter is more commonly used in current practice. Allopurinol requires dose titration, and downward adjustments are needed in patients with renal impairment. Hepatic and renal monitoring is recommended,¹⁴ and rare but serious hypersensitivity reactions (e.g., Steven Johnson's Syndrome) can occur with allopurinol. New treatment options currently in development may offer safer profiles. It is important to remember that these agents should not be initiated in the presence of an acute episode of gout. Most experts recommend that waiting approximately one month after the acute episode is prudent. Additionally, co-administration of low-dose colchicine (0.6 mg p.o. o.d.) or a low-dose NSAID (indomethacin 25 mg p.o. o.d. or b.i.d.) for 3-6 months can be helpful in minimizing flares when the antihyperuricemic agent is being introduced.

Indications for antihyperuricemic therapy include recurrent gouty flares, clinical or radiographic evidence of chronic gout, tophaceous deposition in soft tissue or subchondral bone, gout in the setting of chronic kidney disease, recurrent renal stones, and patients undergoing chemotherapy or radiation therapy.

CONCLUSIONS

Gout can have a significant impact on patient quality of life. Clinicians need to understand that optimal management involves two equally important goals: treatment of the acute flare, and prevention of recurrence (Table 1).¹³ To prevent flares and long-term consequences of untreated gout, at the present time

TABLE 1 Management of Gout

1) Treatment of acute flares

- NSAIDs
- Colchicine
- Oral corticosteroids
- Intra-articular corticosteroids

2) Prevention of recurrence (lowering excess stores of uric acid)

- Uricosuric agents (e.g., probenecid)
- Xanthine oxidase inhibitors
 - allopurinol
 - febuxostat (recently approved in the U.S., to be available soon in Canada)

a uricosuric agent or an inhibitor of XO should be used to bring sUA levels to 360 µmol/L or below. In patients on allopurinol, dose adjustments and renal monitoring should be considered, especially in patients with renal impairment.¹³ Lifestyle modifications can be a useful adjunctive measure in some individuals.

Newer therapies are emerging to provide further options for gout management in the near future, even for patients who have been unable to tolerate current agents or who have had suboptimal responses to them.

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