Avoid perpetuating inequities when managing gout in the setting of COVID-19

PHARMACOTHERAPY

Gout is the most common inflammatory arthritis in New Zealand, but medicines are available to manage and prevent it. This article presents the treatment options available and discusses how COVID-19 might affect prescribing decisions

Leanne Te Karu and Linda Bryant

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Avoiding kaimoana is culturally inappropriate to some people and may not be necessary if gout is well managed

Key points

- There is debate and a lack of clear evidence around the use of prednisone (immunosuppression) and NSAIDs (impact on renal and cardiovascular disease) during this COVID-19 pandemic.
- When introducing urate-lowering therapy, always begin with a "start low, go slow" approach and give gout flare prophylaxis/cover.
- Follow up with patients and continue to reinforce messages at every interaction – check for understanding.
- Treat cardiovascular risk in patients with gout.

It's 8:30 on Tuesday morning and Jack rings telephone triage with yet another gout flare, wanting more diclofenac. He says that he probably had the "wrong food". You note Jack has made multiple similar requests over the years, with requests becoming more frequent – three in the last six months.

Jack is a 39-year-old Māori man with prediabetes and a cardiovascular risk of 5 per cent, with his blood pressure averaging 144/88mmHg over the last year. His estimated glomerular filtration rate (eGFR) is 72ml/min/1.73m^2 and he has microalbuminuria. Although you have previously discussed his cardiovascular risk with him, Jack has not been keen to take any preventive medicines. His weight is 90kg.

A recent article indicated there is inequitable gout treatment in Aotearoa with variation in care for Māori and Pasifika, in whom gout occurs at an earlier age and with worse outcomes compared with non-Māori. In the setting of COVID-19, it is important that inequity gaps are not perpetuated and that a pro-equity approach is applied. Gout is a health condition that can be relatively easily managed to help prevent morbidity and premature mortality.

The ability to provide face-to-face consultation is limited with the current preferred delivery of virtual consults, but Jack has no device or data to enable this. The easy path would be to repeat the diclofenac and flick a script to the pharmacy. You decide to ring Jack so he does not pay for the call, and to revisit gout management with him.

Talking to Jack

As for any health conversation, you start by unravelling Jack's thoughts, beliefs and experience of gout. Even before the COVID-19 lockdown, Jack's employers were becoming frustrated, and he risked losing his job as a labourer. He feels he simply needs larger supplies of diclofenac so he can start taking it before symptoms become debilitating.

In addition, Jack doesn't fully appreciate that while some foods may trigger gout, the actual *cause* is that he has an elevated serum urate level, and there is genetic variation in urate handling. The discussion of genetic differences between Māori and non-Māori provides a better understanding for Jack as to why allopurinol is the gold standard for treating the cause and reducing complications, such as bone deformity, renal disease, cardiovascular disease and tophi – and job loss and relationship problems. You impress upon him that *gout does not go away when the pain goes away*!

Some useful resources that help generate discussion with Jack are shown in Panel 1.

Because beliefs around food have become so entrenched in the general population, you state that focusing on food avoidance is unhelpful, and in the case of kaimoana (shellfish), it is culturally inappropriate to some. However, you discuss fructose with Jack and how ubiquitous it is. Fructose-containing fruit juice increases the risk of gout by 81 per cent, and sweetened soft drink increases risk by 85 per cent, compared with 49 per cent from 15–30g alcohol.[1,2] You add that by lowering his "uric acid" or serum urate level to below 0.36mmol/L, he may be able to enjoy kaimoana again.

Jack has heard of allopurinol and remembers that he has been provided with it previously, but it only made his gout worse. He heard through whānau that allopurinol can be "really bad at making gout worse", so he is not keen to try it again. A quick search shows you that Jack has been prescribed allopurinol twice before. On both occasions, he was not given "cover" (to prevent acute flares) and the starting dose was not matched with his renal function on a "start low, go slow" approach.

You recall that you have also tried getting Jack to come back between gout attacks to start allopurinol but, frustratingly, this has not worked. You establish that there were a few barriers for Jack – his hours of work, transport for getting to the practice, cost of the consult and the prescriptions, and how easy it is to get "gout pills" (usually diclofenac) from friends and whānau in the community. He has bought diclofenac from the pharmacy before, but these are not nearly as strong as the ones you can prescribe. He has also presented to the emergency department before, which mitigated some of the costs.

Gout treatments and COVID-19

Jack's cardiovascular disease risk and microalbuminuria, suggesting endothelial dysfunction, mismanaged gout and prediabetes, don't mean he is at greater risk of becoming infected with COVID-19, but he may experience more severe sequelae if infected.

The acute treatment choices for gout are generally NSAIDs, prednisone or colchicine (Panel 2). You are aware that there have been internet discussions advising against the use of ibuprofen, but none of these are reputable and, beyond the normal cautions, there is nothing robust to validate this.

There is a dose-related 20 to 50 per cent increase in cardiovascular risk with NSAIDs, and they can be nephrotoxic. As Māori and Pasifika generally have a tendency for renal impairment and cardiovascular disease, your approach has been to use short courses of prednisone for first-line treatment of gout. Currently, you worry about prednisone's broad ability to be immunosuppressive. You know that you should not stop it for patients who use it regularly for other rheumatological conditions, but you wonder whether you should use it for gout during the COVID-19 pandemic.

This concern needs to be balanced with attack severity – the most effective treatment should be used, to avoid treatment failure and patients seeking medicines elsewhere, including secondary care. The principle of using the lowest effective dose for the shortest time, rather than "standard" dosing, becomes more crucial. For Jack, the cardiovascular and renal risks are more quantifiable at this time, rather than the unclear impact of prednisone and its immunosuppressive risks.

A "normal" serum urate level during an attack does not exclude gout

Colchicine has been used for millennia for acute treatment of gout, although the dosing has changed considerably in recent times, with fatalities occurring at doses high enough to induce diarrhoea. It is generally slower to provide relief and, as a result, less likely to be used as a first-line treatment.

Recruitment is underway, by the Montreal Heart Institute, for a phase III, multicentre, randomised controlled trial to evaluate the efficacy and safety of colchicine in adult patients diagnosed with COVID-19 (ClinicalTrials.gov: NCT04322682). This is to determine whether short-term treatment with colchicine reduces the rate of death and lung complications related to COVID-19 on the basis of its blood vessel anti-inflammatory properties. This sounds feasible in rationale, but in the absence of any results, no conclusions can be made.

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PANEL 1
Useful learning resources for patients with gout

Health Navigator – www.healthnavigator.org.nz (search for gout)
Gout Happy Feet – https://bit.ly/2UuZNbC
Arthritis New Zealand – www.arthritis.org.nz/gout-arthritis
Pharmac – https://bit.ly/39pX3R2

PANEL 2
Options for acute management of gout

NSAIDs

Naproxen – 750mg initially, followed by 500mg after eight hours, then reduce to 250mg every eight hours until attack has passed.[3]
Diclofenac – 75mg once or twice daily (use for no more than five days at the maximum dose).

Adverse effects of NSAIDs are dose related

Renal – if eGFR is less than 60ml/min, limit the daily dose of diclofenac to 75mg, or naproxen to 1000mg. Be very careful and limit the dose if the patient is on an ACE inhibitor or angiotensin II receptor blocker as well as a diuretic.
Cardiovascular – check the patient's cardiovascular risk calculation and add 20 to 50 per cent (dose-related increase in risk with NSAIDs). It is strongly recommended *not* to give NSAIDs within 24 months of a myocardial infarction or acute coronary syndrome.

Prednisone

Concerns surrounding immunosuppression and unknown risks with COVID-19 mean caution should be taken.

Dose depends on the severity of the gout attack and patient factors, such as size. By dosing at 0.5mg/kg and rounding off this calculation, the dose for Jack would be 40mg for three to five days, then 20mg for up to five days *if needed*.

Tapering the dose over 10 days can reduce the likelihood of a rebound flare, although tapering is not always necessary.

Blood glucose may rise, usually in the late afternoon, but this is transient.

Colchicine (low dose)

Give 1mg stat, followed by 0.5mg one hour later. A further 0.5mg may be taken once or twice daily for two to three more days.[2]

For people less than 50kg or with a creatinine clearance less than 50ml/min, the maximum dosage is 1mg (two tablets) in 24 hours, and no more than 3mg (six tablets) over four days.

Once the maximum cumulative dosage is reached, colchicine should not be used again for at least three days.

The hazards of excessive colchicine need to be stressed to avoid the acute toxicity likely to result from the perception of "more is better".

The dosing approved by the New Zealand Formulary is 1mg (two tablets) immediately, then 0.5mg every six hours, to a maximum of 2.5mg (five tablets) on the first day, a maximum of 1.5mg (three tablets) on subsequent days, and no more than 6mg (12 tablets) in four days.3 Do not repeat the course within three days and use caution with cytochrome P450 3A4 inhibitors.