Fenofibrate – from cholesterol disease to gout?
Dr Lisa Nissen

Gout is a common form of arthritis affecting around 70,000 Australians. It is characterised by recurrent acute attacks of pain, swelling and redness that most commonly affects the joints in the big toe, but gout may also be experienced in the feet, ankles, knees, and less commonly in the elbows, hands and other joints. The symptoms of gout include, intense joint pain (most severe within the first 12 to 24 hours), lingering discomfort (may last days to weeks) and inflammation and redness (with swollen, tender and red joints).

Gout occurs when uric acid builds up in the bloodstream and deposits urate crystals in the joint. The build-up of uric acid is most commonly caused by under-excretion of uric acid by the kidneys, but may also be caused by the overproduction of uric acid by the body. The body produces uric acid when it breaks down purines, substances that are found naturally in the body as well as in certain foods (e.g. meats, anchovies, asparagus, and mushrooms). Other causes of gout can include the use of diuretics, for example, which can cause the retention of too much uric acid.

People are more likely to develop gout if they have high levels of uric acid in their body. There are a number of factors that increase the uric acid level in the body which can include: Lifestyle factors (excessive alcohol use), medical conditions (hypertension, diabetes, cholestererol), certain medications (e.g. thiazide diuretics, low-dose aspirin), family history and sex (more common in men than women), age (men develop it at age 40–60, women after menopause).

Treatment of gout usually involves the use of medications to treat the acute gout attack and to prevent future attacks. Without treatment, an attack will usually resolve within one or two weeks, however with medications the attack can be resolved within several days. There are a number of medications that are used to treat acute attacks, these include non-steroidal anti-inflammatory drugs (NSAIDs) e.g. diclofenac, indomethacin, ibuprofen, and naproxen and more recently COX-2 inhibitors e.g. celecoxib and meloxicam to reduce the inflammation and swelling.

Colchicine, which inhibits urate crystal deposition can be used where NSAIDs are contraindicated to relieve pain in acute gout, however its usefulness is often limited by intolerable side-effects such as nausea, vomiting and diarrhoea. Corticosteroids may also be used where NSAIDs and colchicines cannot be used and can be given either orally or administered as intra-articular injections.

The methods of managing an acute attack of gout differ from the ongoing methods for managing gout. The primary goal in everyday management is to reduce the level of uric acid in the blood so it cannot form crystals in the tissues or joints. The benefits of reducing uric acid in the blood long term include: slowing the progress or risk of kidney disease which may be caused by deposits of urate in the kidneys and possibly reducing the risk of heart disease.

Drugs called xanthine oxidase inhibitors, including allopurinol and febuxostat, limit the amount of uric acid that the body produce lowering the blood’s uric acid level and the risk of gout. However, Xanthine oxidase inhibitors may trigger a new, acute attack if taken before a recent attack has totally resolved. For many patients, for example those with impaired renal function, medications such as allopurinol, cannot be used because of the risk of significant adverse effects or for some patients current gout treatments fail to control their recurrent attacks.

Enter fenofibrate

Fenofibrate is a well established treatment for several types of cholesterol, having first been introduced into clinical practice in the mid-1970s. More recently clinical trials have shown a role for fenofibrate in preventing the progression of coronary artery disease. However of interest to us is the fact that fenofibrate is unique in the fibric acid class of drugs because of its additional ability to lower serum urate. There are a number of case series and small clinical studies that have shown that fenofibrate, when administered for long-term lipid modification, has been associated with marked and sustained reduction in both serum urate levels and acute attacks of gout.

Although fenofibrate does not have a TGA indication for the treatment of gout in Australia, this interesting effect in patients who were treated for lipid modification shows promise and could provide useful add on therapy for patients who have not achieved success with other treatments.

Dosing information

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol</td>
<td>145 mg tablet once daily</td>
</tr>
<tr>
<td>Gout</td>
<td>200 mg–400 mg micronised capsule once daily (Note: 200 mg capsule equivalent to the 145 mg tablet)</td>
</tr>
</tbody>
</table>

Useful References