Prescribing...

For Gout Part 1 Jan 2018

- This month's bulletin revises the management of gout, on the basis of the latest guidelines.
- NSAIDs and colchicine remain the mainstay of treating an acute gout attack.
- Systemic corticosteroids should be restricted to people who don't respond to or who cannot tolerate NSAIDs or colchicine.
- A second bulletin will cover urate lowering therapy.

Background

Gout is the most common form of inflammatory arthritis and its incidence in the UK has steadily increased, from 1.5% in 1997 to 2.5% in 2012. Characterised by deposition of monosodium urate crystals in joints and tissues , it usually presents with intermittent painful attacks followed by long periods of remission. The European League Against Rheumatism (EULAR) and the British Society of Rheumatology (BSR) updated their guidelines on the management of gout in 2017.

The single most important risk factor for gout is sustained hyperuricaemia, which can be caused by overproduction and/or underexcretion of urate. For most people with gout, underexcretion is the main cause of hyperuricaemia. Other factors include drugs (e.g. diuretics, ciclosporin, low-dose aspirin), renal impairment, excessive consumption of red meat or seafood and alcohol (in particular, beer and spirits).

Although the risk of developing gout increases with higher SUA levels, hyperuricaemia alone is not sufficient for diagnosis because most people with hyperuricaemia do not have gout. For example, in healthy, asymptomatic men with SUA levels ≥540µmol/L, the annual incidence rate of gouty arthritis was 5% compared with 0.5% for SUA levels between 416 and 529µmol/L and 0.1% for SUA levels <416µmol/L.9 However, chronic hyperuricaemia is associated with recurrent flares and can lead to tophi, chronic gouty arthritis and erosive arthritis. A definitive diagnosis of gout is made by the demonstration of monosodium urate crystals in synovial fluid.

There have been suggestions of an association between increased SUA levels and various co-morbidities. However, there is no consistent evidence that an elevated SUA level results in coronary heart disease, reduced renal function, hypertension or type 2 diabetes. There is some evidence that a raised SUA level might be associated with worse outcomes in people with cardiovascular and renal disease, so CVD risks should also be assessed.

General advice

Both sets of guidelines emphasise the importance of education, particularly on the benefits, harms and limitations of drug therapy. There is evidence from observational studies of an association between dietary factors and gout development, but high quality evidence from RCTs to either support or refute their use to improve outcomes in people with chronic gout is lacking There is limited evidence that weight loss is associated with a small reduction in SUA levels. Guidelines recommend that, where relevant, patients are provided with evidence based lifestyle advice on exercise, weight management and healthy eating aimed at reducing cardiovascular risk and other related comorbidities.

Treatment of an acute atteck

Drug treatment for an acute attack of gout should be started without undue delay. NSAIDs and colchicine are recommended as first-line treatment options, with corticosteroids generally restricted to those people who don't respond to, or cannot tolerate, NSAIDs or colchicine.

1. **Non-steroidal anti-inflammatory drugs (NSAIDs)**

   Although guidelines recommend using NSAIDs for acute gout flares, the authors of a large Cochrane review (23 trials, 2,200 participants) found limited evidence supporting their use in the treatment of gout. In terms of pain relief, there was some evidence that systemic glucocorticoids and NSAIDs were equally beneficial. There is no evidence of differences between different NSAIDs in patients with gout.

2. **Colchicine**

   A Cochrane review (2 trials, 124 participants) found low-quality evidence that high-dose colchicine is likely to be an effective treatment for acute gout. Compared with placebo, high- and low dose colchicine reduced pain but higher doses were associated with more gastrointestinal adverse effects. In one trial, low-dose colchicine (1.2mg followed by 0.6mg one hour later; total 1.8mg) compared with high-dose colchicine (1.2mg followed by 0.6mg every hour for 6 hours; total 4.8mg) resulted in similar efficacy but greater tolerability (diarrhoea 23% vs. 77%; severe diarrhoea 0% vs. 19%). Several guidelines recommend using a low-dose regimen of colchicine. The BSR guideline suggests a dose of colchicine 0.5mg two to four times daily, but recognises that higher doses are often associated with gastrointestinal adverse effects. In the UK, the licensed dose of colchicine is 1mg followed by 0.5mg after 1 hour; after 12 hours treatment can resume with a maximum dose of 0.5mg 8 hourly until symptoms are relieved with no more than 6mg per course and at least 3 days between courses.

   In people with moderate renal impairment, a lower starting dose or longer duration between doses is recommended. In patients with normal renal or liver function who are taking cytochrome P450 3A4 inhibitors (e.g. ritonavir, clarithromycin, itraconazole, ketaconazole, diltiazem) or p-glycoprotein inhibitors (e.g. ciclosporin), the dose of colchicine should be reduced by 50% or 75%, depending on the interacting drug. There have been case reports of myopathy and rhabdomyolysis associated with the use of colchicine in people with renal impairment who were also taking simvastatin or atorvastatin.

3. **Corticosteroids**

   A Cochrane review (3 studies, 148 patients) did not find clinically relevant differences between the systemic corticosteroids studied and the comparator drugs (e.g. diclofenac, indometacin). No serious adverse effects were reported from short-term use of systemic corticosteroids. EULAR and BSR guidelines recommend a short course (3–5 days) of an oral corticosteroid (30–35mg/day prednisolone) in patients unable to tolerate NSAIDs or colchicine. Although there is no evidence from randomised trials to support the use of intra-articular corticosteroid injections in acute gout, clinical experience and expert opinion suggests that such injections can be helpful, particularly in gout affecting single joints or where comorbidity precludes other treatments. In patients where monotherapy is insufficient for treating acute flares, a combination of NSAIDs with either intra-articular corticosteroids, oral steroid or colchicine may be used.

4. **Interleukin-1 inhibitors**

In a Cochrane review (four studies, 806 participants) a single dose (150mg) of canakinumab was shown to produce marginal improvements when compared with a single suboptimal dose (40mg) of triamcinolone acetonide given by intramuscular injection. Canakinumab treatment is very expensive (£9,928/dose). NICE has not published guidance on its use and no application has yet been received by PBAC to review it locally.

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References : Drugs and Therapeutics Bulletin , January 2018