

arthritis and ankylosing spondylitis, biological therapies have been proven to be highly effective in the treatment of these diseases.⁵⁻⁷

Conclusion

There is a window of opportunity for highly successful treatment of RA in the first year and especially in the 3 months after diagnosis. This is a crucial step in achieving optimal control of disease progression and functional status. The use of optimal treatment in early RA is essential. Patients who do not achieve rapid disease control on standard DMARD therapy should be considered for biological therapy. Studies have shown better radiographic outcome and disease activity control on these agents.

However, it is unfortunately likely that health economic issues will dominate the determination of future optimal therapeutic regimens for early RA, psoriatic arthritis, juvenile idiopathic arthritis and ankylosing spondylitis.

References available on request.

MANAGEMENT OF GOUT

M M T M ALLY, MB BCh, FCP (SA)
Rheumatologist, University of Limpopo, MEDUNSA Campus

The burden of hyperuricaemia (HU) and its related disorders is significant and increasing among black South Africans against a background of a 24.4% prevalence of hypertension, improving socio-economic conditions and changing lifestyle and dietary habits.

HU is defined as a serum uric acid (S-UA) > 0.42 mmol/l in men and > 0.36 mmol/l in women. However, the most important factor is the degree of solubility. As the level rises above 0.42 mmol/l, the tendency for crystallisation and precipitation in joints and soft tissue increases, resulting in clinical disease. Other factors such as acidic pH, decreased temperature, dehydration and trauma also influence solubility adversely.

Table 1. Primary and secondary hyperuricaemia

Primary Increased production Decreased excretion (90% of cases)
Secondary Increased production Haematological malignancies High-purine diet/alcohol Chemotherapy
Decreased excretion Hypertension Renal failure Drugs (diuretics, low-dose aspirin, pyrazinamide/ethambutol) Acidosis Dehydration

HU is divided into an asymptomatic phase, acute gouty arthritis, the inter-critical period, chronic tophaceous gout and urolithiasis. Comorbid diseases such as hypertension, ischaemic heart disease, obesity, type 2 diabetes mellitus, insulin resistance, hyperlipidaemia and hypothyroidism are important and require appropriate treatment. Uric acid is produced as the breakdown product of purines. HU occurs when there is a primary or secondary problem with either overproduction or underexcretion (Table 1).

Management of the HU depends on the clinical phase of the disease.

Asymptomatic HU

Only 20% of patients with increased S-UA develop gout or renal stones; therefore not all patients need specific urate-lowering drugs (ULDs). Dietary restriction of purine is impractical and only lowers S-UA marginally (± 0.06 mmol/l). A low caloric diet addressing obesity and insulin resistance seems to be more appropriate. Red meat, some seafoods and alcohol, especially beer and spirits, should be avoided. Dairy products have been shown to be protective and vegetable proteins are not problematical.

If S-UA levels are > 0.72 mmol/l in men and > 0.58 mmol/l in women introduction of ULDs should be considered. Treatment is lifelong, and as

compliance is a major problem patient education and co-operation are important.

Acute flare-up

Fifty per cent of patients present typically with a monoarthritis affecting the 1st metatarsophalangeal joint, the



It's the **shell** that makes **Ecotrin** safer.

Safety-Coated
Ecotrin[®]
81mg

The miracle of Aspirin made **safer**.

Each tablet contains Aspirin 81mg. Reg.No.: 29/2.7/0767
Pharmafrica (Pty) Ltd, 33 Hulbert Road, New Centre, Johannesburg 2001
Under licence from Goldshield Pharmaceuticals Ltd. U.K.

swollen, erythematous, tender joint mimicking cellulitis or septic arthritis. A low-grade fever may be present. Of note is that the S-UA may be normal initially. However, most patients will have an elevated S-UA after 4 weeks. It is important to make a definitive diagnosis with aspiration of fluid or tophus to demonstrate UA crystals. However, laboratory experience in detecting crystals may vary and the clinical, serological and radiological picture can assist in making a presumptive diagnosis to initiate treatment.

An acute attack maybe precipitated by factors that elevate UA, but drugs used to lower UA could also precipitate a flare-up. Therefore, never start these drugs during an acute attack. If the patient already has chronic gout and an acute flare-up occurs, these drugs should be continued.

The main focus of treatment is to relieve pain and inflammation using colchicine or non-steroidal anti-inflam-

matory drugs (NSAIDs) and in some cases steroids. These drugs have no effect on the S-UA level.

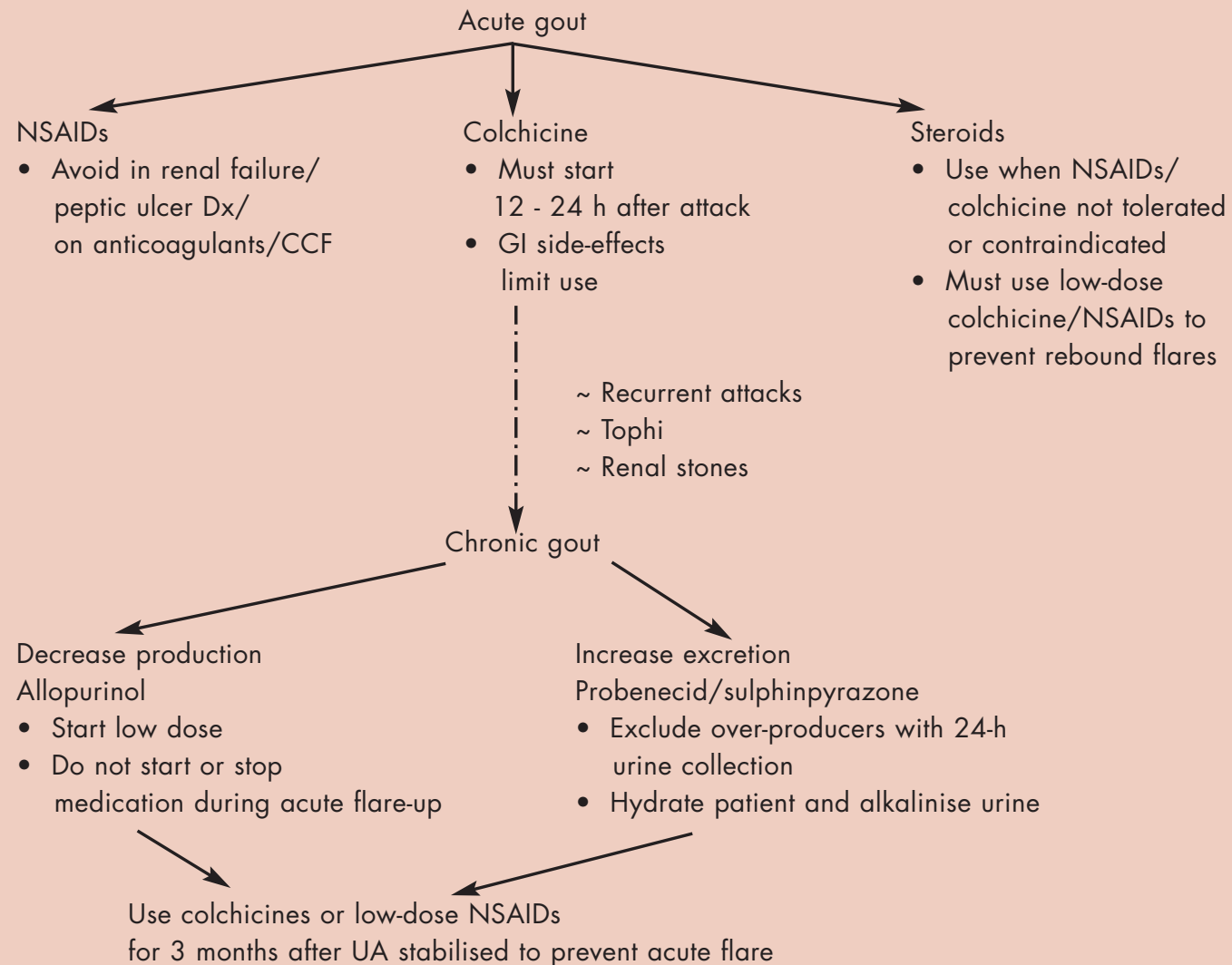
NSAIDs

More important than the choice of NSAIDs, is their prompt use. The maximum prescribed dose should be given initially, then tapered once symptoms improve. They must be avoided in patients with renal failure, congestive cardiac failure, active peptic ulcer disease or in those on anticoagulation.

Colchicine

This needs to be given early – within 12 - 24 hours of the attack. There is a poor response if it is given > 48 hours after the attack. The starting dose is 1 mg followed by 0.5 mg 1 - 2 hourly until a maximum of 6 mg is reached or gastrointestinal side-effects such as diarrhoea, abdominal cramps, nausea and/or vomiting develop. These side-effects occur commonly, thus limiting its use. Intravenous colchicine should be avoided as the potential for serious adverse effects exists.

Treatment algorithm



Steroids

Intra-articular steroids are useful and effective if only 1 - 2 joints are involved. In polyarticular involvement where NSAIDs/colchicine is contraindicated, intramuscular or oral steroids are alternatives, e.g. prednisone 0.5 mg/kg daily, weaning over 7 - 10 days. It is important to use low-dose NSAIDs or colchicine to prevent rebound flare-up once steroids are discontinued.

Intercritical period (between flares)

After the initial flare-up the patient may remain asymptomatic for many years. Therefore there is no need for ULDs, but over time these asymptomatic periods become shorter.

Chronic gout

This is characterised by more than 2 acute attacks per year with progression to polyarticular involvement and soft-tissue deposition, called tophi. It may also be complicated by renal stones.

The main focus of management is to lower S-UA levels gradually once acute joint symptoms have settled for at least 2 weeks.

Prophylactic colchicines 0.5 mg 1 - 2 times per day or low-dose NSAIDs need to be given for 6 weeks after the S-UA is stabilised at a level of < 0.3 mmol/l.



Two important groups of ULDs act either by decreasing production or increasing excretion.

Decreasing production

Allopurinol, a xanthine-oxidase inhibitor, is used in most cases because of ease of administration. The daily dosage is 100 - 900 mg (average dose 300 mg daily). Start at a low dose and increase after 2 - 4 weeks until the desired UA level is reached. Dosage requires adjustment if there is associated renal dysfunction. Fever and rashes may herald severe toxic syndrome requiring withdrawal of the drug.

Increasing excretion (uricosuric agents)

These agents promote uric acid excretion but require normal renal function and over-producers need to be excluded with a 24-hour urine UA collection. If excretion is > 800 mg - 1g per day uricosuric agents cannot be used, as this could result in renal stones. Alkalise urine to prevent renal stones. Uricosuric agents can occasionally be combined with allopurinol.

Probenecid

The dose is 250 mg bd up to 500 mg bd. You can use up to 1 g bd but ensure urinary excretion is not > 800 mg/day.

Sulphinpyrazone

This dose is 50 - 200 mg tds, but this drug is not available in South Africa.

Benzbromarone

Benzbromarone has been discontinued because of hepatic side-effects. The low-dose benzbromarone and allopurinol combination has also recently been discontinued.

Other agents

Fenofibrate, a lipid-lowering agent, has been shown to have a mild uricosuric effect.

Losartan, an angiotensin II receptor antagonist, reduces S-UA level and raises urinary pH, thus simultaneously preventing stone formation.

Practice points

- Confirm diagnosis with crystal identification.
- Address comorbidities, especially obesity and insulin resistance.
- Consider patient compliance before starting treatment.
- Never start ULDs during an acute attack of gout and do not stop ULDs if a patient with chronic gout develops an acute flare-up.
- Be wary of drugs causing secondary gout and dosage adjustments in renal dysfunction.
- Lower uric acid gradually.

References available on request.

ANTIPHOSPHOLIPID ANTIBODIES AND SYNDROMES: RELEVANCE FOR THE GP

RONALD A ASHERSON, MB ChB, MD (Hon), FRCP, FCP (SA)
Consultant Rheumatologist,
Rosebank Clinic, Johannesburg

With the discovery of the anticardiolipin antibodies in 1983 and subsequent research on the antiphospholipid antibodies over the ensuing 20 years, many of the clinical events and paradoxes in this field before this time have been explained. Although a positive lupus anticoagulant test (a functional clotting test performed by most laboratories) was at first thought to be due to the presence of interfering antibodies against phospholipids, an integral part of the clotting process, it has since been shown that these antibodies are directed against proteins. The binding of phospholipid to certain domains on one protein in particular (beta 2 glycoprotein 1 (β2GP1), one of the body's natural anticoagulants) alters the conformation of peptides at certain positions on the molecule, forming what is known as a cryptic epitope or neoantigen against which the antiphospholipid antibodies are directed (Fig. 1).

Between 5% and 8% of normal individuals produce antibodies to phospho-