777FM.3 MANAGEMENT OF GOUT

BACKGROUND

Gout is the most common cause of inflammatory arthritis worldwide, and its incidence, prevalence and severity is increasing in the UK[1]. Untreated gout causes chronic disability and reduced quality of life. Despite effective treatments, gout is still often misdiagnosed and its management remains suboptimal[1].

DIAGNOSIS OF GOUT

Presentation

Acute gout presents with an abrupt onset of pain, swelling and erythema, most commonly (up to 78% of first attacks) affecting the great toe (podagra). Other joints that are frequently affected include midfoot, ankle, knee, wrist, finger and elbow. The common triggers include a direct trauma to the joint, dehydration, intercurrent illness, surgery and high alcohol intake in preceding 48 hours.

The following clinical features are highly suggestive of gout:

- First metatarsophalangeal (MTP) joint involvement.
- Rapid onset of severe joint pain over 6 - 12 hours.
- Joint swelling and tenderness and overlying erythema.
- Self-limiting with complete resolution.
- Tophus (proven or suspected).

The differential diagnosis includes septic arthritis, calcium pyrophosphate dihydrate (CPPD) arthritis (pseudogout), occasionally rheumatoid arthritis (RA) or psoriatic arthritis (PsA)[2].

Risk factors for gout

- Male gender.
- Older age >65 years.
- Genetic factors (reduced renal clearance of urate).
- Loop and thiazide diuretics, ciclosporin, low dose aspirin.
- Chronic kidney disease.
- Dietary factors - excessive alcohol beer/spirits, purine rich foods (such as red meat, offal, shellfish, herring, sardines, yeast extracts), fructose, sugar-sweetened drinks.

Investigations

1. Full blood count (FBC) and C-reactive protein (CRP). *Gout will cause an inflammatory response, however a raised white cell count (WCC) would suggest an infective cause.*
2. Joint aspiration. *The gold standard for diagnosis is demonstration of uric acid crystals in the joint aspirate or tophus material. However, a typical presentation in a patient without evidence of another cause of inflammatory arthritis is sufficient.*
3. Serum urate. *Measurements are often normal during an attack and need to be repeated 4 - 6 weeks after the acute attack settles.*
4. Renal function. *This will guide treatment options.*
5. Lipid profile, HbA1c. *Screening for associated comorbidities and cardiovascular risk factors is essential.*
6. X-rays, may see chondrocalcinosis (CPPD), chronic gouty changes. (Punched out erosions, intra-osseous lesions, sclerotic overhanging edges, periarticular osteopenia)[2].

MANAGING AN ACUTE ATTACK

Overarching principles

1. Treat early. (Colchicine is most effective if given within 12 hours of onset of flare.)
2. Continue urate lowering therapy (ULT) if already established - **do not stop.**
3. Every person with gout should be fully informed about the disease, the existence of effective treatments, associated comorbidities and the principles of self-managing acute attacks[3].
4. Every person with gout should receive life style advice:
    a. weight loss if appropriate
    b. avoidance of alcohol and sugar-sweetened drinks
    c. limit excessive intake of meat and seafood
    d. Low-fat dairy products should be encouraged
    e. Regular exercise should be advised[4]
5. Medication review - if taking a diuretic for hypertension then consider another anti-hypertensive. Losartan has uricosuric properties. Consider switching furosemide to bumetanide.
6. Every person with gout should be screened for associated comorbidities and cardiovascular risk factors, including renal impairment, coronary heart disease, obesity, hyperlipidemia, hypertension, diabetes and smoking[3].

Therapeutic options

Evidence shows that colchicine/NSAIDs/corticosteroids are comparably as effective. First line treatment should be based on patient choice, co-morbidities, concomitant medication, number and type of joints involved[3].

1. Colchicine
    - Dose is 500 micrograms PO BD – TDS.
    - Maximum dose is often limited by gastrointestinal side effects, most frequently diarrhoea. The usual maximum is 6 mg per course. A second course should not be commenced for 3 days. [NOTE: longer courses of twice daily colchicine can be used for longer periods – see p3.]
    - Contraindicated if estimated glomerular filtration rate (eGFR) <10.
    - Use lower doses if eGFR 10 - 50, and in the elderly (once or twice daily).
    - Caution and low doses only in those taking statins, cimetidine, erythromycin, fluoxetine, azole antifungals, tolbutamide.
    - Avoid co-prescription of clarithromycin or ciclosporin.
2. Non-steroidal anti-inflammatory drugs (NSAIDs) - see guideline 299FM for choices.
    - Co-prescribe a proton pump inhibitor (PPI) - see guideline 656FM.
3. Prednisolone
    - 20 - 30 mg PO OD for 3 - 5 days.
4. Intra-articular corticosteroid – consider in monoarthritis.
5. Combination therapy[3].

Review at 4 - 6 weeks

Repeat serum uric acid and renal function.
Assess lifestyle factors (diet, exercise, alcohol, sugary drinks).
Assess cardiovascular risk factors (obesity, hypertension, lipids and diabetes).
Offer urate lowering therapy to everyone after first flare[4].

URATE LOWERING THERAPY (ULT)

The aim of ULT is reduce and maintain serum uric acid levels at or below a target level of <0.3 mmol/L. This prevents further urate crystal formation and dissolves away existing crystals.

Urate lowering therapy should be discussed and offered to **all patients** with a diagnosis of gout but is especially important in those patients with:

- 2 or more attacks of gout over 12 months
- Tophaceous gout or gouty erosions on X-ray
- Uric acid renal stones
- Chronic kidney disease (CKD) and gout
- Continuing diuretics (e.g. heart failure) and gout

Use NSAID + PPI cover or colchicine 500 micrograms PO once to twice daily until 6 weeks after target serum uric acid levels are achieved to prevent acute attacks that are common after initiating urate lowering therapy.

Start allopurinol once acute attack has been treated.

1) Perform pre-treatment blood tests: Uric acid, FBC, urea and electrolytes (U&Es), liver function tests (LFTs).
2) Provide information booklet on allopurinol and explain potential side effects. https://www.versusarthritis.org/media/1343/allopurinol-information-booklet.pdf
3) Start on low dose of allopurinol 100 mg PO OD.
4) Check U&Es and uric acid every 2 - 4 weeks and increase dose of allopurinol in 100 mg increments until uric acid levels <0.3 mmol/L (TREAT TO TARGET).
5) Usual dose required is between 300 - 400 mg/day, maximum dose 900 mg a day (if normal renal function).
6) Lower starting doses of allopurinol are to be used in patients with renal impairment:

eGFR <5	50 mg/week
eGFR 5 - 15	50 mg twice weekly
eGFR 16 - 30	50 mg every 2 days
eGFR 31 - 60	50 mg/day
eGFR >60	100 mg/day[2]

If allopurinol not tolerated or target uric acid level not achieved:

Consider febuxostat (Amber initiation):

Febuxostat is a selective xanthine oxidase inhibitor, it is licensed for treatment of chronic hyperuricaemia where uric acid deposition has already occurred[6].

1) Check there are no contraindications including; ischaemic heart disease (IHD), congestive cardiac failure (CCF), pregnancy, breastfeeding, concomitant use of azathioprine or mercaptopurine, severe hepatic impairment. Note that in a phase 4 clinical study in patients with gout and a history of major cardiovascular (CV) disease, a significantly higher risk for all-cause mortality and for CV related death was observed in patients treated with febuxostat[7].
2) Perform pre-treatment blood tests: uric acid, FBC, U+Es, LFT and thyroid function tests (TFTs) (if has known thyroid disease).
3) Provide information booklet and explain potential side effects: https://www.versusarthritis.org/media/1349/febuxostat-information-booklet.pdf.
4) Start on dose of 80 mg PO OD.
5) Check FBC, LFTs and uric acid after 2 - 4 weeks and increase to 120 mg PO OD if uric acid not in target range (<0.3 mmol/L).
6) Can cause raised LFTs in 5% of patients, if alanine aminotransferase test (ALT) elevated >2 upper limit normal check for other causes, if none found then stop febuxostat.
7) Monitor TFTs in patients with known thyroid disease and adjust doses as needed.
8) Anaemia, thrombocytopaenia or pancytopaenia occur rarely - if FBC abnormal stop febuxostat[6].

Consider a uricosuric agent e.g.

- Sulfinpyrazone (200 - 800 mg/day)[amber initiation] or probenecid (unlicensed) (500 - 2000 mg/day PO) in patients with normal or mildly impaired renal function.
- Benzbromarone (unlicensed) (hospital only - on a named patient basis; 50 - 200 mg/day PO) in patients with mild to moderate renal insufficiency[6].

If target serum uric acid not achieved on monotherapy:

A uricosuric agent can be used in combination with a xanthine oxidase inhibitor.

Severe refractory tophaceous gout:

Refer to Rheumatology.

Ongoing monitoring after starting treatment

Allopurinol **Probenecid**	Uric acid and U&Es every 3 - 4 weeks until uric acid level <0.3 mmol/L and the dose is stable. Then U&Es, uric acid, ALT and alkaline phosphatase (ALP) 3 monthly for the first year and 6 monthly thereafter. In stable patients, annual checks may be appropriate in due course.
Febuxostat	Uric acid every 2 - 4 weeks until target <0.3 mmol/L is reached. If target level reached monitor uric acid every 6 months in the first year and then annually thereafter. Do LFTs and FBC at the same time as uric acid levels in the first year of treatment [6].
Sulfinpyrazone	Uric acid and U&Es every 3 - 4 weeks until uric acid level <0.3 mmol/L achieved and the dose is stable. FBC, U&Es, uric acid, ALT and ALP 3 monthly for the first year and 6 monthly thereafter.
Benzbromarone	Uric acid, U&Es and ALT and alk phos every 3 - 4 weeks until uric acid level <0.3 mmol/L achieved and the dose is stable. FBC, U&Es, uric acid, ALT and ALP 3 monthly for the first year and 6 monthly thereafter.

A patient information leaflet on gout can be downloaded from:
https://www.versusarthritis.org/media/1253/gout-information-booklet.pdf

References

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See also:
BHT Pol 071 Medicines Policy, Annexe 4 - Unlicensed Medicines Policy (BHT users only)
Guideline 299FM Prescribing Non-steroidal Anti-inflammatory Drugs in Adults
Guideline 656FM Use of Proton Pump Inhibitors
Guideline 781FM Febuxostat

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