ACUTE HOT JOINT, SEPTIC ARTHRITIS AND GOUT
Supporting information

This guideline has been prepared with reference to the following:

NICE. Gout: diagnosis and management. 2022. NICE. London

https://www.nice.org.uk/guidance/ng219

Hui M, Carr A, Cameron S et al. The British Society for Rheumatology Guideline for the Management of Gout. Rheumatology (Oxford). 2017;56:e1-e20

https://academic.oup.com/rheumatology/article/56/7/e1/3855179

Immediate treatment

Analgesia should begin with diclofenac 50 mg orally 8 hrly, plus paracetamol 1 g orally 6 hrly if required, plus codeine phosphate 60mg 6 hrly if required, and then changed if necessary to morphine sulphate solution 10 mg orally 4 hrly?

Diclofenac is as effective as (although no more so than) other NSAIDs for the treatment of pain due to inflammatory rheumatic conditions, but has the advantage of causing fewer and less serious gastrointestinal side-effects than aspirin or indometacin (Sutaria, 2006; Kim, 2004).

Several studies have indicated that supplementation of an NSAID with paracetamol is more effective than giving higher doses of the NSAID alone (Seideman, 1993 i,ii,iii), and reduces the risk of side effects.

A systematic review including 19 placebo-controlled trials of codeine in addition to paracetamol in 1204 patients (Moore, 1997) found that the NNT to achieve a 50% or greater level of pain relief was 3.1 with the addition of codeine 60mg, vs 5.0 with paracetamol 600/650mg alone. A meta-analysis of 80 RCTs (Zhang, 1996) found similar results, in that only the combination of 600mg paracetamol with 60mg codeine was more effective than paracetamol alone. No marked dose-response relationship was seen in doses ranging from 500-1500mg.

Oral morphine is often used as a last resort because of fear of the possibility of habituation and dependency. A randomised double-blind crossover study (Moulin, 1996) of 46 patients has established that doses of up to 120 mg daily over a period of nine weeks in patients with intractable pain of soft-tissue or musculoskeletal origin carry a low risk of addiction and improve pain intensity scores. On visual analogue scales, the morphine group showed a reduction in pain (p=0.01) compared to placebo over the first 3 weeks.

Kim KY, Schumacher HR, Hunsche E, et al. A literature review of the epidemiology and treatment of acute gout. Clin Ther 2003;25:1593-1617

Moore A, Collins S, Carroll D, et al. Paracetamol with and without codeine in acute pain: a quantitative systematic review. Pain 1997;70;193-201

Moulin DE, Iezzi A, Amireh R, et al. Randomised trial of oral morphine for chronic non-cancer pain. Lancet 1996;347:143-7

Seideman P. (i) Additive effect of combined naproxen and paracetamol in rheumatoid arthritis. Br J Rheumatol 1993;32:1077-82
http://rheumatology.oxfordjournals.org/content/32/12/1077.long

Seideman P. (ii) Paracetamol in rheumatoid arthritis. Agents Actions Suppl 1993;44:7-12

Seideman P. (iii) Naproxen and paracetamol compared with naproxen only in coxarthrosis. Increased effect of the combination in 18 patients. Acta Orthop Scand 1993;64:285-8

Sutaria S, Katbamna R, Underwood M. Effectiveness of interventions for the treatment of acute and prevention of recurrent gout: a systematic review. Rheumatology 2006;45:1422-31
http://rheumatology.oxfordjournals.org/content/45/11/1422.long

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Zhang WY, Li Wan Po A. Analgesic efficacy of paracetamol and its combination with codeine and caffeine in surgical pain: a meta-analysis. J Clin Pharm Ther 1996;21:261-82

Evidence Level: Diclofenac – II (In rheumatoid arthritis/osteoarthritis); Paracetamol – III; Codeine – I; Morphine - II

Oral prednisolone 10 mg daily is indicated for patients already taking low dose steroids?
Severe recurrent stress of any type (e.g. infection) may precipitate adrenal crisis in patients whose endogenous cortisol secretion has been suppressed by previous glucocorticoid therapy (Cronin, 1997; Streeten, 1996). As the major pathophysiological event precipitating acute adrenal crisis is mineralcorticoid deficiency, and as prednisolone exhibits minimal mineralcorticoid activity, additional steroid cover is necessary (Cronin, 1997).
A Cochrane systematic review of 3 trials in 148 patients (Janssens, 2008) found that patients with gout did not report any serious adverse effects after taking short-term systemic corticosteroids.
A 5 day course of prednisolone may also be a cost –effective treatment (Cattermole, 2009).

Cattermole GN, Man CY, Cheng CH, et al. Oral prednisolone is more cost-effective than oral indomethacin for treating patients with acute gout-like arthritis. Eur J Emerg Med 2009;16:261-6

Cronin CC, Callaghan N, Kearney PJ, et al. Addison disease in patients treated with glucocorticoid therapy. Arch Intern Med 1997;157:456-8

Janssens HJ, Lucassen PL, Van de Laar FA, et al. Systemic corticosteroids for acute gout. Cochrane Database Syst Rev. 2008, Issue 2. Art. No.: CD005521
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005521.pub2/full

Streeten DH, Anderson GH, Bonaventura MM. The potential for serious consequences from misinterpreting normal responses to the rapid adrenocorticotropin test. J Clin Endocrinol Metab 1996;81:285-90

Evidence Level: V

Staphylococcus aureus is the commonest implicated microbe in septic arthritis?
Staphylococcus aureus is responsible for 60-80% of adult non-gonococcal bacterial arthritis (Nade, 2003). A UK study of 74 cases seen over a period of 10 years isolated the organism from 81% (Cooper, 1986).

Cooper C, Cawley, MI. Bacterial arthritis in an English health district: A 10 year review. Ann Rheum Dis 1986;45:458-63
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1001917/pdf/annrheumd00273-0018.pdf

Nade S. Septic arthritis. Baillieres Best Pract Res Clin Rheumatol 2003;17:183-200

Evidence Level: IV

Sodium fusidate 500 mg orally 8 hrly plus EITHER flucloxacillin OR (if allergic to penicillin) clindamycin is appropriate for patients with intact immune systems, with no other inflammatory arthritis and with only 1 joint involved?
Sodium fusidate is particularly effective against staphylococcus aureus and resistance is uncommon (Anderson, 1980). Because of the possibility of resistant organisms forming at low doses, it is usually given in combination with another antibiotic (Verbist, 1990). In a randomised trial (Mehtar, 1995) of 56 patients with serious gram-positive infections (mostly *S. aureus* or *S. epidermis*), 8 of 9 (89%) treated with flucloxacillin and sodium fusidate 500 mg orally 8 hrly were “clinical successes” (defined as cure plus improvement). The overall bacteriological eradication rate was 74% for teicoplanin, 67% for flucloxacillin alone and 88% for flucloxacillin plus fusidic acid. There are a limited number of definitive clinical studies of the use of sodium fusidate in bone and joint infection and several of these were conducted in children, were not designed to analyse the benefit of the drug over other antibiotics, or did not include an adequate comparison group (Atkins, 1999).

Anderson JD. Fusidic acid: new opportunities with an old antibiotic. CMAJ 1980, 122:765-9
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1801889/pdf/canmedaj01131-0033.pdf

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Atkins B, Gottlieb T. Fusidic acid in bone and joint infections. Int J Antimicrob Agents 1999;12:S79-S93

Mehtar S, Drabu Y, Wilson AP, et al. A comparative study between teicoplanin alone and flucloxacillin, plus or minus fusidic acid, in the treatment of serious infections caused by methicillin-susceptible gram-positive bacteria. Chemotherapy 1995;41:412-9

Verbist L. The antimicrobial activity of fusidic acid. J Antimicrob Chemother 1990;25(Suppl B):1-5
http://jac.oxfordjournals.org/content/25/suppl_B/1.full.pdf+html

Evidence Level: II

Subsequent management

In septic arthritis, antibiotics should be continued for 6 weeks, or longer if joint not settled?
No clinical studies to determine the optimum duration of antimicrobial therapy for septic arthritis have yet been carried out (Nade, 2003; Kortekangas, 1999). Advice is usually to continue until the joint is free of pain when weight-bearing, is unswollen, and laboratory indicators of infection have returned to normal, which may take several weeks (Kortekangas, 1999). In practice, the usual minimum duration is 2 weeks of iv followed by 4 weeks of oral therapy (Anon, 2003).
A 2023 retrospective review of 137 adult patients diagnosed with native joint septic arthritis found that compared with the remission group, the relapse group showed a significantly higher proportion of cases that received antibiotic therapy for <= 4 weeks (4.8% vs. 46.2%, p < 0.001) [Joo, 2023]. The authors concluded that patients with native joint septic arthritis require vigilant monitoring for relapse, particularly when treated with antibiotic regimens administered for less than four weeks.

Anon. The management of septic arthritis. Drug Ther Bull 2003;41:65-8

Kortekangas P. Bacterial arthritis in the elderly: an overview. Drugs Aging 1999;14:165-71

Joo EJ, Kim B, Sohn KM et al. Administering Antibiotics for Less Than Four Weeks Increases the Risk of Relapse in Culture-Positive Septic Arthritis of Native Joints. J Clin Med. 2023;12:6808
https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/37959273/

Nade S. Septic arthritis. Baillieres Best Pract Res Clin Rheumatol 2003;17:183-200

Evidence Level: V

In confirmed gout, colchicine 0.5 mg orally 6 hrly should be used if NSAIDs are contraindicated?
A 2021 systematic review of RCTs found evidence that low-dose colchicine may be an effective treatment for acute gout when compared to placebo that its benefits may be similar to NSAIDs (McKenzie, 2021). This review identified 4 RCTs with 803 randomised participants. The number of people who reported treatment success (50% or greater pain reduction) at 32 to 36 hours was slightly larger with low-dose colchicine (418 per 1000) compared with placebo (172 per 1000; risk ratio (RR) 2.43, 95% confidence interval (CI) 1.05 to 5.64). The incidence of total adverse events was 364 per 1000 with low-dose colchicine compared with 276 per 1000 with placebo: RR 1.32, 95% CI 0.68 to 2.56. No participants withdrew due to adverse events or reported any serious adverse events. A single RCT comparing high-dose to low-dose colchicine indicated there may be little or no difference in benefit in terms of treatment success at 32 to 36 hours but more adverse events associated with the higher dose.
ACR (2012) recommend an initial dose of 1 mg, followed by 500 mcg every 2-3 hours, to a maximum of 6 mg.
In the first controlled study of colchicine in acute gout (Ahern, 1987), two-thirds of 43 patients experienced some pain relief (>= 50% over the baseline score on a visual analogue scale) within 18 hours, compared with one-third given placebo. In all patients given colchicine however, toxicity in the form of gastrointestinal disturbances occurred and in 91% this was experienced before major improvements in the pain score. For this reason, colchicine is only appropriate for use in patients unable to take NSAIDs (Kim, 2003).

American College of Rheumatology. ACR Guidelines for the Management of Gout. Part 2: Therapy and Antiinflammatory Prophylaxis of Acute Gouty Arthritis. 2012.

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http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3662546/

Ahern MJ, Reid C, Gordon TP, et al. Does colchicine work? The results of the first controlled study in acute gout. Aust NZ J Med 1987;17:301-4

Kim KY, Schumacher HR, Hunsche E, et al. A literature review of the epidemiology and treatment of acute gout. Clin Ther 2003;25:1593-1617

McKenzie BJ, Wechalekar MD, Johnston RV et al. Colchicine for acute gout. Cochrane Database Syst Rev. 2021 Aug 26;8(8):CD006190
https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD006190.pub3/full

Evidence Level: II

Allopurinol should not be started in acute gout?

Historically, there has been concern that starting urate-lowering therapy such as allopurinol could worsen or prolong the acute gout flare, however a 2016 review of the evidence found that this is not an issue. Based on evidence from two RCTs, it is reasonable to start allopurinol during an acute flare of gout when combined with acute gout treatment as this does not prolong the flare. A 2021 systematic review found no significant association between all-cause mortality and allopurinol use in people with gout (Hay, 2021).

Hay CA, Prior JA, Belcher J et al. Mortality in Patients With Gout Treated With Allopurinol: A Systematic Review and Meta-Analysis. Arthritis Care Res (Hoboken). 2021;73:1049-54
https://onlinelibrary.wiley.com/doi/10.1002/acr.24205

Robinson PC, Stamp LK. The management of gout: Much has changed. Aust Fam Physician. 2016;45:299-302
http://www.racgp.org.au/afp/2016/may/the-management-of-gout-much-has-changed/

Evidence Level: I

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