THE JOURNAL OF FAMILY PRACTICE

ONLINE EXCLUSIVE

Cochrane Musculoskeletal Group review: Acute gout

Steroids or NSAIDs? Let this overview from the Cochrane Group help you decide what's best for your patient.

Tania Winzenberg, MBBS, FRACGP, PhD
Menzies Research Institute, Hobart, Tasmania, Australia
Tania.Winzenberg@utas.edu.au

Rachelle Buchbinder, MBBS, MSc, PhD, FRACP
Monash Department of Clinical Epidemiology, Cabrini Institute, Melbourne, Victoria, Australia

Gout afflicts about 2% of men over age 30 and women over age 50 and its prevalence appears to be increasing.[1] In the United States in 2005, an estimated 3 million adults had suffered an episode of gout in the preceding year.[2] Health care utilization costs associated with the disorder are substantial.[3]

Options for treating acute gout include nonsteroidal anti-inflammatory drugs (NSAIDs), colchicine, and intra-articular and systemic corticosteroids.[4] Choosing among them can be challenging, however, because the evidence that one or another of these options yields real benefit is of varying strength. Using NSAIDs can be problematic with increasing age, as comorbidities like gastrointestinal (GI) bleeding, renal failure, heart failure, and cardiovascular risk increase and anticoagulant therapy is more likely to be in use.[5] That's where the kind of systematic reviews Cochrane Musculoskeletal Group (CMSG) performs can be of real help.

Colchicine and steroids: What the reviews tell us

The CMSG has done 2 systematic reviews of acute gout therapy. In 1, Schlesinger and colleagues went over all the available clinical trials to assess the efficacy and adverse effects of colchicine compared to placebo or to other acute gout treatments.[6] In the other, Janssens

IN THIS ARTICLE

Test your skills with 2 cases
Page E3

How this series can help you

This article is the first in a series intended to bring the findings of the Cochrane Musculoskeletal Group (CMSG) to the attention of family physicians.

CMSG—one of the largest review groups that comprises the Cochrane Collaboration—includes more than 200 active researchers, health care professionals, and consumer representatives from 26 countries. The group synthesizes the results of high-quality clinical trials to determine whether interventions for the prevention, treatment, and rehabilitation of musculoskeletal disorders are safe and effective. Each article in this series will summarize a CMSG review on a single topic, using common clinical scenarios to demonstrate how the information the review supplies can be applied to clinical practice.

and colleagues performed a similar review to assess the efficacy and safety of systemic corticosteroids in the treatment of acute gout in comparison with placebo, other acute gout treatments, or no therapy.[7]

Colchicine. Only 1 randomized controlled trial (RCT) of colchicine was identified.[6] The trial included 43 participants (mostly men) who were treated with either colchicine or placebo, and the effects of treatment in both groups were compared. Colchicine was given as an initial dose of 1 mg orally followed by 0.5 mg every 2 hours until the acute episode subsided or toxic side effects occurred.

All 22 participants who took colchicine developed diarrhea or vomiting within 24 hours of initiating therapy, after taking a mean dose of 6.7 mg. In other words, the number needed to harm from colchicine therapy given in this way was 1. Three patients had to be treated in order to achieve at least a 50% decrease in pain.

No RCTs comparing colchicine with other treatments of acute gout were found. Case reports suggest that lower doses (0.5 mg, 3 times a day or less) of colchicine may be associated with fewer GI side effects, but there was no RCT evidence to support this approach.[8]

Systemic corticosteroids. No placebo-controlled trials of either intra-articular or systemic corticosteroids were found. Three trials involving 148 patients compared different systemic corticosteroids with different control drugs.[7]

Intramuscular (IM) triamcinolone acetonide 60 mg was compared with oral indomethacin 50 mg 3 times daily in 1 trial, and with IM adrenocorticotropic hormone (ACTH) 40 IU in a second trial. In a third trial, oral prednisolone (30 mg daily for 5 days) was compared with an initial single IM injection of 75 mg diclofenac followed by oral indomethacin 50 mg 3 times a day for 3 days, and then a reduced dose of 25 mg indomethacin 3 times a day for another 3 days.

No clinically relevant differences between the corticosteroids and the comparator drugs were found in any of the 3 trials. No important safety problems were attributed to the corticosteroid medications. Most adverse events were related to the comparator drugs—in particular to the NSAIDs. In view of the low quality and variability in the design of the trials, the review authors could not draw firm conclusions about the comparative effectiveness of systemic corticosteroids and the other drugs used.

Another study comes on heels of Cochrane review

A further RCT in progress at the time of the review compared oral prednisolone 35 mg daily with naproxen 500 mg twice daily for 5 days in 120 patients. This trial has since been published.[9] It was a double-blind, double-dummy RCT with adequate allocation concealment, low loss to follow up, and thus low risk of bias.[10] The results showed that the 2 interventions were clinically equivalent, with a 73% and 78% decrease in pain score over 90 hours in the prednisolone and naproxen groups, respectively. Most of the improvement occurred during the first 42 hours. Adverse events did not differ between groups.

Design the therapy to fit the patient

The study cited above demonstrates that there is no real difference, either in efficacy or safety, between corticosteroids and NSAIDs in the treatment of gout. In theory, that would seem to mean that you could feel equally comfortable prescribing either therapy. But in clinical practice, characteristics of individual patients and the profile of each class of drugs will influence your choice. The following cases illustrate this point. These cases discuss the initial treatment of acute gout, but of course in clinical practice you would go on to consider ongoing prophylactic treatment.

FAST TRACK

All 22 participants who took colchicine developed diarrhea or vomiting within 24 hours of initiating therapy.

CASE 1

Mr. Peters is a 53-year-old man with a body mass index of 29. He is usually well and not on any medication. He limps into your office one day, complaining of excruciating pain in his left great toe that started suddenly the night before. He'd had a bad night, with pain so severe he couldn't even tolerate the pressure of the bed sheet on his foot. A dose of acetaminophen failed to control the pain. He has never experienced anything like it.

You look at his foot, and find a swollen, erythematous first metatarsophalangeal joint. On the basis of this classic presentation, you make a provisional diagnosis of gout.

Q. What immediate treatment do you choose?

You consider colchicine, but decide against it because of its side effect profile. Mr. Peters has no contraindication for NSAIDs, so you start him on diclofenac 50 mg orally, 3 times a day. You are aware that NSAIDs can have adverse effects in some patients. If Mr. Peters develops these or fails to improve quickly on diclofenac, you will consider switching him to intra-articular or systemic corticosteroids. Therefore, you ask him to check back with you in 48 hours regarding his progress. At this review, you find his symptoms are settling well, with no adverse effects.

CASE 2

Mrs. Jones, age 81, arrives in your waiting room with an acutely painful, red, and swollen right index finger. Her condition makes it very difficult for her to bathe and prepare meals, a serious problem because she lives alone. She has hypertension, chronic atrial fibrillation, and chronic mild heart failure that has been stable for more than a year.

Mrs. Jones takes warfarin 4 mg daily because of her atrial fibrillation. Her international normalized ratio (INR) has been stable on this dose for the last 6 months. Mrs. Jones also takes perindopril 5 mg and hydrochlorothiazide 6 mg daily for her heart failure and hypertension. Her renal function is normal.

You notice that in addition to the inflamed proximal interphalangeal joint of the index finger of the right hand, Mrs. Jones has swelling and what appears to be a tophus over the distal interphalangeal joint of the third finger, which suggests that she has gout. You realize that the thiazide diuretics may have precipitated this problem and that possibility will need to be addressed, but in the short term you are concerned about managing her pain and restoring her hand function.

Q. What treatment do you consider?

There are many reasons why you are extremely reluctant to use NSAIDs. Mrs. Jones's age and the warfarin she takes create an unacceptably high risk of GI bleeding. Other side effects of NSAIDs, including hypertension and fluid retention, could aggravate her cardiac failure. You are also reluctant to use colchicine at the recommended high dosage for acute gout, because the GI effects associated with this drug may further incapacitate Mrs. Jones, and because the risk of dehydration with or without renal failure is particularly serious in an elderly woman.

You could consider a lower dose of colchicine, but the evidence for effectiveness and rapid onset of action at lower doses is weak and information on the frequency of GI effects at lower doses is not available. While a short course of oral corticosteroids is a possibility, these drugs also carry a risk of GI bleeding when used in combination with warfarin and might worsen her cardiac failure.

A steroid injection is worth considering. No RCTs have examined the effectiveness and safety of intra-articular corticosteroids for gout, but an uncontrolled trial of intra-articular triamcinolone acetonide (10 mg to the knee and 8 mg into small joints) demonstrated pain relief within 48 hours in all 19 patients receiving this treatment.[4,11] Further, there is evidence that intra-articular corticosteroids are effective in other inflammatory joint conditions. Intra-articular injection of a corticosteroid carries a small risk of joint hemorrhage in a patient taking warfarin

FAST TRACK

One RCT found that oral prednisolone 35 mg daily and naproxen 500 mg twice daily were clinically equivalent.

and might be painful when administered into the finger, but if the injection is done carefully with a small needle, this seems to be the safest option. You decide to explain the risks and benefits of the different strategies for treating gout, and recommend a local corticosteroid injection.

Q. If you're not experienced in this technique and a rheumatologist or other specialist is not immediately available to perform it for you, what would you do then?

Because Mrs. Jones's heart failure is stable and mild, you can consider a 5-day course of prednisolone together with a proton pump inhibitor to reduce the risk of GI toxicity while monitoring her heart failure and INR carefully. While the dose of prednisolone used in the trials was 30 to 35 mg, you are reluctant to use a dose this high with this patient, and so opt to use a lower dose of 15 mg daily and review her progress in 24 hours. The next day her symptoms are improved and Mrs. Jones continues the prednisolone for the next 4 days.

FAST TRACK

NSAIDs are a reasonable first option, provided there are no contraindications.

So where do we go from here?

Although anti-inflammatories, colchicine, and intra-articular and systemic corticosteroids have been mainstays of treatment for acute gout for years, evidence to guide your therapeutic choices is limited. NSAIDs are a reasonable first option, provided there are no contraindications. However, as Case 2 illustrates, when NSAIDs are contraindicated the available evidence provides only limited guidance for treatment choices.

While colchicine has demonstrated efficacy at the standard dosage of 1 mg orally followed by 0.5 mg every 2 hours, the unacceptably high level of GI side effects, together with concerns about more serious toxicity, limits its usefulness.[12] No trials have examined the effectiveness and safety of lower doses. Intra-articular corticosteroids may be effective, but this has not been tested in an RCT.

One trial found that oral prednisolone 35 mg daily provided equivalent relief to NSAIDs, and this is another treatment option.[9] However, it is unclear whether lower doses of oral corticosteroids might be similarly effective with reduced risks. The bottom line is that more high-quality clinical trials are needed to determine the optimum therapy for acute gout. ■

Correspondence

Tania Winzenberg, MBBS, Menzies Research Institute, Private Bag 23, Hobart, Tasmania, Australia 7001; Tania.Winzenberg@utas.edu.au

Disclosure

The authors reported no potential conflict of interest relevant to this article.

References

1. Choi HK, Curhan G. Gout: epidemiology and lifestyle choices. *Curr Opin Rheumatol*. 2005;17:341-345.
2. Lawrence RC, Felson DT, Helmick CG, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. *Arthritis Rheum.* 2008;58:26-35.
3. Wu EQ, Patel PA, Yu AP, et al. Disease-related and all-cause health care costs of elderly patients with gout. *J Manag Care Pharm*. 2008;14:164-175.
4. Zhang W, Doherty M, Bardin T, et al. EULAR evidence based recommendations for gout. Part II: Management. Report of a task force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). *Ann Rheum Dis*. 2006;65:1312-1324.
5. *Australian Medicines Handbook*. 9th ed. Adelaide, Australia: Australia Pty Ltd; 2007.
6. Schlesinger N, Schumacher R, Catton M, et al. Colchicine for acute gout. *Cochrane Database Syst Rev.* 2006;(4):CD006190.
7. Janssens HJ, Lucassen PL, Van de Laar FA, et al. Systemic corticosteroids for acute gout. *Cochrane Database Syst Rev*. 2008;(2):CD005521.
8. Morris I, Varughese G, Mattingly P. Colchicine in acute gout. *BMJ.* 2003;327:1275-1276.
9. Janssens HJ, Janssen M, van de Lisdonk EH, et al. Use of oral prednisolone or naproxen for the treatment of gout arthritis: a double-blind, randomised equivalence trial. *Lancet*. 2008;371:1854-1860.
10. Juni P, Altman DG, Egger M. Systematic reviews in health care: assessing the quality of controlled clinical trials. *BMJ*. 2001;323:42-46.
11. Fernandez C, Noguera R, Gonzalez JA, et al. Treatment of acute attacks of gout with a small dose of intraarticular triamcinolone acetonide. *J Rheumatol*. 1999;26:2285-2286.
12. Australian Adverse Drug Reactions Committee and the Adverse Drug Reactions Unit of the Therapeutic Goods Administration. Fatal interactions and reactions with colchicine: beware CYP3A4 inhibitors. Australian Adverse Drug Reactions Bulletin October 2008. Available at: http://www.tga.gov.au/adr/aadrb/aadr0810.htm#a1. Accessed June 1, 2009.