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Priority Updates from the Research Literature from the Family Physicians Inquiries Network

Acute gout: Oral steroids work as well as NSAIDs

Prednisone is a safe and effective alternative when NSAIDs are contraindicated

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Practice changer

Use a short course of oral steroids (prednisone 30-40 mg/d for 5 days) for treatment of acute gout when nonsteroidal anti-inflammatory drugs (NSAIDs) are contraindicated. Steroids are also a reasonable choice as first-line treatment.[1,2]

Strength of recommendation
B: 2 good-quality, randomized controlled trials (RCTs)

Janssens HJ, Janssen M, van de Lisdonk EH, van Riel PL, van Weel C. Use of oral prednisolone or naproxen for the treatment of gout arthritis: a double-blind, randomized equivalence trial. *Lancet.* 2008;371:1854-1860.

Man CY, Cheung IT, Cameron PA, Rainer TH. Comparison of oral prednisolone/paracetamol and oral indomethacin/paracetamol combination therapy in the treatment of acute goutlike arthritis: a double-blind, randomized, controlled trial. *Ann Emerg Med.* 2007;49:670-677.

ILLUSTRATIVE CASE

A 68-year-old man with a history of ulcer disease and mild renal insufficiency comes to your office complaining of severe pain in his right foot. You note swelling and redness around the base of the big toe and diagnose acute gout. Wishing to avoid nonsteroidal anti-inflammatory drugs (NSAIDs) and colchicine because of the patient's medical history, you wonder what you can safely prescribe for pain relief.

NSAIDs have become the mainstay of treatment for acute gout,[3,4] replacing colchicine—widely used for gout pain relief since the early 19th century.[5] Colchicine fell out of favor because it routinely causes diarrhea and requires caution in patients with renal insufficiency.[6] Now, however, there is growing concern about the adverse effects of NSAIDs.

Comorbidities, age, mean fewer options

NSAIDs increase the risk of gastrointestinal (GI) bleeding, especially in the first week of use.[7] Cyclooxygenase-2 (COX-2) inhibitors, considered as effective as NSAIDs in treating acute gout pain,[8] are also associated with GI bleeds.[9] In addition, NSAIDs and COX-2 inhibitors increase cardiovascular risks, prompting the American Heart Association to recommend restricted use of both.[10] NSAIDs' effect on renal function, fluid retention, and interactions with anticoagulants are additional concerns, because gout patients are generally older and often have comorbid renal and cardiovascular diseases.[3,11-13]

CONTINUED

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PURLs® INSTANT POLL

Do you routinely prescribe prednisone (or other oral steroids) for acute gout?

- ❑ Yes, but only when other treatments are contraindicated.
- ❑ Yes, it's my preferred treatment.
- ❑ No, I have never prescribed oral steroids for acute gout.

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FAST TRACK

Although prednisone is prescribed for gout only 9% of the time, evidence suggests it's a good alternative to NSAIDs

PURLs methodology

This study was selected and evaluated using FPIN's Priority Updates from the Research Literature (PURL) Surveillance System methodology. The criteria and findings leading to the selection of this study as a PURL can be accessed at www.jfponline.com/purls.

In the United States, nearly 70% of patients who develop acute gout seek treatment from primary care physicians.[12] Family physicians need a safe alternative to NSAIDs to relieve the severe pain associated with this condition. Will oral corticosteroids fit the bill?

STUDY SUMMARIES

Oral steroids: A safe and effective alternative

Janssens et al[1] conducted a double-blind, randomized equivalence trial of 118 patients to compare the efficacy of prednisolone and naproxen for the treatment of monoarticular gout, confirmed by crystal analysis of synovial fluid. The study was conducted in the eastern Netherlands at a trial center patients were referred to by their family physicians. Those with major comorbidities, including a history of GI bleed or peptic ulcer, were excluded.

Participants were randomized to receive either prednisolone 35 mg* or naproxen 500 mg twice a day, with look-alike placebo tablets of the alternate drug, for 5 days. Pain, the primary outcome, was scored on a validated visual analog scale from 0 mm (no pain) to 100 mm (worst pain experienced).[15] The reduction in the pain score at 90 hours was similar in both groups. Only a few minor side effects were reported in both groups, and all completely resolved in 3 weeks.

The study by Man et al[2] was a randomized trial that compared indomethacin with oral prednisolone in 90 patients presenting to an emergency department in Hong Kong. Diagnosis of gout was made by clinical impression. Participants in the indomethacin group also received an intramuscular (IM) injection of diclofenac 75 mg, and those in both groups were monitored for acetaminophen use as a secondary endpoint.

Pain reduction, the primary endpoint, was assessed with a 10-point visual analog score, and was slightly better statistically in the oral steroid group. The study was not designed to evaluate for safety, but the authors noted that patients in the indomethacin group experienced more adverse effects (number needed to harm [NNH] for any adverse event: 3; NNH for serious events: 6).

Short-term steroids have few side effects

In both studies, patients receiving oral steroids experienced no significant side effects. This finding is consistent with other studies that have investigated short-term oral steroid use in the treatment of both rheumatoid arthritis and asthma.[16,17]

WHAT'S NEW?

Evidence supports use of steroids for acute gout

In the United States, prednisone is prescribed as treatment for acute gout only about 9% of the time.[12] These 2 studies—the first randomized trials comparing oral steroids with NSAIDs, the usual gout treatment—may lead to greater use of steroids for this painful condition.

Both studies were well designed and conducted in an outpatient (or emergency) setting. Both showed that a short course of oral steroids is as effective as NSAIDs, and without significant side effects.

Previous studies have compared IM steroids with NSAIDs, and IM steroids with IM adrenocorticotropic hormone (ACTH).[18,19] However, these studies were not blinded—just one of their methodological problems.[4]

CAVEATS

Joint aspiration is not the norm

In the Janssens study, participants were diagnosed with gout after monosodium urate crystals were found in joint aspirate.[1] This may not be the usual practice in primary care settings, where a clinical diagnosis of gout is typically made. The

*Prednisone is the precursor of prednisolone and is activated in the liver. The activity of both drugs is comparable, and prednisone and prednisolone can be converted milligram to milligram. However, prednisolone may be preferred for patients with severe liver disease.[14] (In the United States, prednisolone is available as a liquid and prednisone as a tablet.)

authors indicate that the failure to perform joint aspiration will lead to occasional cases of septic arthritis being treated with oral steroids. We recommend joint aspiration or a referral for such a procedure when clinical evidence (eg, fever and leukocytosis) is suggestive of septic arthritis.

Possible impact of acetaminophen

In the study by Man et al, acetaminophen was used by both groups as an adjunct for pain relief, and the amount used was higher (mean 10.3 g vs 6.4 g over 14 days) in the oral steroid group. It is possible that some of the pain relief experienced by those in the steroid group may have been from acetaminophen; however, a difference of 4 g over a 14-day period makes that unlikely. Even if additional acetaminophen is required, the advantages of oral steroids rather than NSAIDs or colchicine for patients with contraindications remain.

Also of note: These trials examined short-term treatment of acute gout. These findings cannot be extrapolated to the treatment of intercurrent gout or chronic gouty arthritis, since long-term steroid use has severe adverse effects.

CHALLENGES TO IMPLEMENTATION

No significant barriers

We found little to prevent physicians from adopting this practice changer. Oral steroids are readily available and inexpensive, and most primary care clinicians regularly prescribe them for other conditions. This practice change recommendation should be readily implemented. ■

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FAST TRACK

Patients with fever and leukocytosis—suggestive of septic arthritis—should undergo joint aspiration before being treated with oral steroids for acute gout