

Gout Guidelines Highlight Risk Factor Analysis

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The optimal treatment for gout requires both pharmacologic and nonpharmacologic therapy to reduce the severity of acute attacks and prolong the period between them, according to new gout management guidelines issued by the European League Against Rheumatism.

The guidelines and accompanying set of diagnostic recommendations are similar to the quality care indicators for gout published in 2004 (*Arthritis Rheum.* 2004;50:937-43), said Dr. Kenneth Saag, director of the University of Alabama's Center for Education and Research on Therapeutics of Musculoskeletal Disorders, Birmingham. The indicators are used mostly by researchers of quality of care issues.

Dr. Saag said that clinical guidelines for gout treatment are needed because, with more people using long-term thiazide diuretics and people with chronic illness generally living longer, the incidence of gout is increasing.

EULAR commissioned a 20-member panel that included 11 rheumatologists and 1 expert in evidence-based medicine to develop the guidelines. It drew its management recommendations from a review of 181 studies published from 1945 to 2005.

The recommendations are graded according to a formula that includes risk/benefit tradeoffs. Expert commentary accompanies those recommendations that reflect standard clinical practice but lack significant supporting research (*Ann. Rheum. Dis.* 2006;65:1312-24).

Treatment in all stages of gout should be tailored to specific risk factors (serum urate level, radiographic evidence), clinical phase (acute, intercritical, or chronic), and general risk factors (gender, age, obesity, alcohol use, urate elevating drugs, and other comorbidities), according to the guidelines. Nonpharmacologic treatments are also important, because they can potentiate drugs' effectiveness, are inexpensive, and do not cause harmful or distressing side effects.

The EULAR panel's recommendations for managing gout include the following:

- ▶ Patients should reduce alcohol and purine-rich food consumption and lose weight if they are obese.
- ▶ Hyperlipidemia, hypertension, hyperglycemia, obesity, and smoking should also be addressed. The link between metabolic syndrome and elevated serum uric

acid has been proved in clinical studies. There is no direct evidence linking smoking to gout, but smoking has been associated with increased alcohol consumption, thereby having an association with gout.

- ▶ During acute gout, oral colchicine and/or nonsteroidal anti-inflammatory drugs should be the first-line treatment. Patients who cannot tolerate the GI effects of colchicine, however, can be treated with NSAIDs which provide gastroprotection.

- ▶ A 1-g loading dose of colchicine followed by 0.5 mg every 2-3 hours relieves symptoms in acute attacks, but even this level may cause serious GI side effects. A lower dose (0.6 mg three times per day) may be appropriate and effective, but there are no studies addressing this.

- ▶ Neither intra-articular aspiration nor injection of long-acting steroids has been studied in controlled trials. However, case reports and uncontrolled trials indicate

that the treatments are well tolerated and effective in reducing pain. They may be especially important for patients who cannot tolerate pharmacotherapy.

- ▶ Only patients with recurrent acute attacks, arthropathy, tophi, or radiographic changes should receive urate-lowering drugs. There is little agreement on whether less severe patients should have long-term urate-lowering therapy. However, all gout patients should make urate-lowering lifestyle changes through diet modification.

- ▶ A uric acid level of less than 6 mg/dL—below the saturation point for monosodium urate—should be the target serum level. Many patients with serum uric acid in the normal range can still have joint damage. Maintaining the lower level keeps crystals from precipitating into the joints.

- ▶ "Start low, go slow" with allopurinol for long-term urate-lowering therapy. To avoid the rare but potentially life-threatening al-

lopurinol hypersensitivity syndrome, begin with 100 mg/day and increase by 100 mg/day every 2-4 weeks.

- ▶ Patients with normal renal function who cannot tolerate allopurinol may do well with a uricosuric drug such as probenecid or sulphinpyrazone. For renal patients, benzbromarone can be tried, but liver function should be carefully monitored.

- ▶ Low-dose colchicine (0.5-1.0 mg daily) and/or NSAIDs may have a place in preventing additional attacks. One placebo-controlled trial suggested that colchicine could prevent half of acute attacks, although all colchicine-treated patients experienced diarrhea. Evidence suggests that NSAIDs are not as effective.

- ▶ If possible, stop diuretic therapy in gout patients. Replace the diuretic with another antihypertensive; losartan and fenofibrate are effective and have modest uricosuric effects. ■

Diagnostic Criteria Draw On Research and Expert Opinion

The presence of monosodium urate monohydrate crystals in synovial fluid remains the gold standard for gout diagnosis, with a sensitivity of 84% and a specificity of 100%, according to new gout diagnostic guidelines issued by the European League Against Rheumatism.

But the crystals may be present only during an acute attack, and their identification requires a clinician who is both well trained and experienced, the document notes. Additionally, the cost-effectiveness of the test has not been fully demonstrated (*Ann. Rheum. Dis.* 2006;65:1301-11).

The guidelines put forth 10 diagnostic criteria for gout, ranked not only upon extant research but also on benefit and risk, cost, and the clinical expertise required to effectively use the criteria.

"This seems a better system, reflecting both research evidence and expert opinion, than the traditional semiautomatic estimation based on category of research data alone," wrote Dr. Weiya Zhang of the University of Nottingham (England), who led a 20-person panel in developing the document.

The recommendations were drawn from the same 181 studies, published from 1945 to 2005, from which the EULAR panel drew its 12 gout man-

agement recommendations (see accompanying story).

The recommendations address clinical, biochemical, and radiographic diagnostic techniques for the disease:

1. Clinical symptoms of rapidly developing severe joint pain and swelling, especially with overlying erythema, are highly indicative of crystal formation but have low sensitivity (23%) for a gout diagnosis without further evidence.

2. Monosodium urate monohydrate (MSU) crystals in synovial aspirate have both high sensitivity and high specificity, although variability in lab expertise may affect the accuracy of the sample findings.

3. A clinical diagnosis of classic recurrent podagra with hyperuricemia can be reasonably assumed to be gout but requires MSU crystal confirmation.

4. All patients with inflamed joints should have their synovial fluid examined for MSU crystals.

5. MSU testing can also be performed between bouts of inflammation, because urate crystals persist in intercritical periods in up to 70% of patients.

6. Because gout and sepsis may occur simultaneously, all possible gout patients should also have Gram staining and culture of synovial fluid. The test should be performed even if the fluid is

positive for MSU crystals, because septic arthritis can progress rapidly and carries a significant risk of morbidity and mortality.

7. Serum uric acid can't be used exclusively as a diagnostic tool. Many people with high serum uric acid don't develop gout, and some patients with confirmed MSU crystals have normal serum uric acid.

8. Gout patients under age 25 years who have a family history of the disease or who have renal calculi should have a 24-hour urinary uric acid/creatinine ratio done. The 24-hour screen appears to be more accurate and cost effective than an early morning spot sample.

9. Radiographs might be useful for a differential diagnosis, but they can't confirm gout. There are radiographic changes in all stages of gout, but many affected joints can be radiographically normal. Patients with intradermal tophi are more likely to show severe radiographic changes.

10. Male gender, diet, alcohol use, and diuretics increase the risk of gout, but don't ignore other important risk factors. These include hypertension (relative risk of 4, compared with controls), coronary heart disease (odds ratio, 1.75), chronic renal failure (odds ratio, up to 5), and obesity (odds ratio, 3.8).

Diacerein Found More Effective Than NSAIDs in Osteoarthritis

Diacerein has advantages over placebo and nonsteroidal anti-inflammatory drugs in treating hip and knee osteoarthritis, according to a new meta-analysis.

Diacerein is a member of the symptomatic slow-acting drugs in osteoarthritis group. They are of interest because they reduce cartilage degradation while improving symptoms. They tend to start working slowly, but they

have a prolonged residual effect after treatment is stopped.

For the meta-analysis, published in the Sept. 25, 2006, issue of *Archives of Internal Medicine*, Dr. Bernhard Rintelen and colleagues from the Lower Austrian Center for Rheumatology, Stockerau, Austria, analyzed 19 randomized controlled trials involving a total of 2,637 patients (*Arch. Intern. Med.* 2006;166:1899-906).

Eight of the trials were placebo controlled, while 11 had active controls, which mainly compared diacerein with nonsteroidal anti-inflammatory drugs (NSAIDs).

During the active treatment phase, diacerein was significantly superior to placebo in reducing pain and improving function, with a Glass score (standardized mean difference) of 1.50, the authors wrote. NSAIDs showed similar

efficacy to diacerein during active treatment, but at treatment end, diacerein's efficacy lasted up to 3 months longer, whereas NSAIDs did not (Glass score of 2.06).

Diacerein seemed well tolerated, even after long-term use. The most common adverse event was mild to moderate diarrhea, starting in early treatment and resolving during continuing therapy. The only other frequent adverse

event was darker-than-normal urine, which had no clinical significance. There were no statistically significant differences between diacerein and NSAIDs in tolerability, though patients taking NSAIDs had a greater number of severe events. Diacerein is marketed as Artrodar in India, Europe, and Latin America. It is not yet available in the United States.

—Robert Finn