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This series is coordinated by Corey D. Fogleman, MD, Assistant Medical Editor.

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Colchicine for Acute Gout

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Clinical Question

Should colchicine be used to treat acute gout?

Evidence-Based Answer

Low-quality evidence shows that low-dose colchicine (up to 1.8 mg over one hour) is an effective therapy for acute gout. However, it has not been compared with nonsteroidal anti-inflammatory drugs (NSAIDs) or corticosteroids in clinical trials. Concerns include high cost, drug-drug interactions, and potential toxicity. (Strength of Recommendation: B, based on inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

Colchicine is an alkaloid inhibitor of microtubule formation derived from the meadow saffron or autumn crocus in the Northern Hemisphere. It has been used since ancient times for medicinal purposes. In 2009, after sponsoring a small randomized controlled trial, URL Pharma received exclusive rights to produce colchicine (Colcrys) for gout and the much rarer disease, familial Mediterranean fever. As a result, the price increased 50-fold from about $0.10 to $5.00 per pill.[1]

This Cochrane review updates a 2006 meta-analysis of a single study of 43 people. A second industry-sponsored study of 185 people was added to the current review. Both were randomized controlled trials. In the more recent study, the authors compared a high-dose colchicine regimen to a low-dose regimen. The high-dose regimens in the two studies—which included a 1- to 1.2-mg loading dose, followed by either 0.6 mg every hour for six hours or 0.5 mg every two hours until therapeutic response or intolerance (i.e., nausea, vomiting, or diarrhea)—caused significantly more adverse effects (number needed to treat to harm = 2). The shorter, low-dose regimen of 1.2 mg, followed by 0.6 mg in one hour (followed by placebo every hour for five hours) was as effective as the higher dosages in the more recent study, but with adverse effects similar to those in the placebo group. Using an outcome of at least 50% pain reduction at 24 to 32 hours with low-dose colchicine vs. placebo, the number needed to treat for the low-dose regimen was five.

No trials compared colchicine with other interventions (e.g., NSAIDs, corticosteroids). Most participants in these two studies were men, and this Cochrane review does not address whether colchicine is beneficial after the first two days of an exacerbation.

The 2012 American College of Rheumatology guidelines for managing gout state that low-dose colchicine is equal to NSAIDs and corticosteroids for treating acute gout.[2] For severe acute gout, colchicine may be used with NSAIDs or corticosteroids. The guidelines call for at least six months of anti-inflammatory prophylaxis while starting urate-lowering therapy to prevent gout flare-ups, and slightly favor colchicine in a dosage of 0.6 mg once to twice daily in this regard.

The dose of colchicine should be reduced for patients with severe renal or hepatic disease. There is a 1% risk of reversible axonal neuromyopathy in patients taking colchicine; colchicine can cause rhabdomyolysis when used with statins or clarithromycin (Biaxin); and colchicine has multiple drug-drug interactions with cytochrome P3A4 inhibitors, including certain antiviral agents, antifungal agents, calcium channel blockers, and grapefruit.[3,4] Comparative studies among the different treatments for acute gout and for flare-up prophylaxis are needed.

SOURCE: van Echteld I, et al. Colchicine for acute gout. *Cochrane Database Syst Rev.* 2014;(8):CD006190.

The practice recommendations in this activity are available at http://summaries.cochrane.org/CD006190.

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Aclidinium for Stable COPD

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Clinical Question

In adults with stable chronic obstructive pulmonary disease (COPD), does aclidinium (Tudorza Pressair) decrease exacerbations and mortality or improve quality of life?

Evidence-Based Answer

Aclidinium did not decrease all-cause mortality or exacerbations requiring oral steroids, antibiotics, or both. However, aclidinium decreased the number of patients with exacerbations requiring hospitalization and improved quality of life in those with stable COPD. (Strength of Recommendation: A, based on consistent, good-quality patient-oriented evidence.)

Practice Pointers

COPD is the third leading cause of death in the United States after cardiovascular disease and malignancy.[1] COPD costs $30 billion in direct expenditures and $20 billion in indirect expenditures, such as those associated with work absenteeism and disability.[2] As a mainstay of therapy, long-acting bronchodilators are recommended for the treatment of patients with significant symptoms or at high risk of exacerbations.[3] The authors looked at the use of aclidinium, an M3 muscarinic receptor–selective, long-acting anticholinergic medication, for the treatment of patients with COPD.

This Cochrane review included 12 randomized controlled trials with 9,547 patients who had stable COPD. Aclidinium did not impact all-cause mortality when compared with placebo (odds ratio [OR] = 0.92; 95% confidence interval [CI], 0.43 to 1.94), nor did it decrease the incidence of exacerbations requiring steroids, antibiotics, or both (OR = 0.88; 95% CI, 0.74 to 1.04). Aclidinium was associated with fewer exacerbation-related hospitalizations (OR = 0.64; 95% CI, 0.46 to 0.88; number needed to treat [NNT] = 77; 95% CI, 51 to 233) over the length of the studies (from four to 52 weeks). More patients taking aclidinium reported a clinically significant improvement in quality of life when compared with placebo (OR = 1.49; 95% CI, 1.31 to 1.70; NNT = 10; 95% CI, 8 to 15), and more patients reported an improvement in dyspnea (OR = 1.73; 95% CI, 1.52 to 1.98). Serious adverse events were similar between aclidinium and placebo (OR = 0.89; 95% CI, 0.70 to 1.14). Fewer people in the aclidinium group withdrew because of a lack of effectiveness (OR = 0.31; 95% CI, 0.23 to 0.43), although aclidinium was associated with increased reports of diarrhea (OR = 2.32; 95% CI, 1.14 to 4.74).

Aclidinium was also compared with tiotropium (Spiriva), another long-acting muscarinic antagonist. There were no deaths in the head-to-head trials, no statistically significant difference in exacerbations requiring steroids or antibiotics, and no difference in exacerbations requiring hospitalization. No differences were noted in nonfatal serious adverse events between the two medications. Aclidinium is dosed twice daily, whereas tiotropium is given once daily.

The Global Initiative for Chronic Obstructive Lung Disease recommends smoking cessation, physical activity, and influenza and pneumococcal vaccination for all patients with COPD.[3] Pharmacotherapy is recommended to reduce symptoms and improve exercise tolerance.[3] As with other long-acting muscarinics, aclidinium is a well-tolerated option for the pharmacologic management of persons with COPD who experience significant symptoms or are at high risk of exacerbations.

SOURCE: Ni H, et al. Aclidinium bromide for stable chronic obstructive pulmonary disease. *Cochrane Database Syst Rev.* 2014;(9):CD010509.

The practice recommendations in this activity are available at http://summaries.cochrane.org/CD010509.

The views expressed here are those of the author and do not necessarily reflect those of the U.S. Army or the Department of Defense.

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