

## **Does Colchicine Improve Pain in an Acute Gout Flare?**

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### **Take-Home Message**

Low-quality evidence suggests that both high- and low-dose colchicine decreases pain in acute gout flares; however, high-dose regimens are associated with more frequent adverse effects.

### **Methods**

#### **Data Sources**

In this review, the authors searched the Cochrane Central Register of Controlled Trials to April 2014, MEDLINE (1948 to April 2014), and EMBASE (1980 to April 2014). They reviewed the 2010 to 2013 American College of Rheumatology and the European League against Rheumatism conference proceedings. In addition, [clinicaltrials.gov](http://clinicaltrials.gov) and the WHO trials register were searched.

#### **Study Selection**

The authors included all randomized controlled trials and controlled clinical trials on the benefits and harms of colchicine in adult patients with acute gout flares, identified by the presence of monosodium urate crystals in joint aspirate or patients fulfilling standard criteria. The major outcomes included benefits, defined as 50% or greater reduction in pain at 12, 24, 36, or 48 hours; reduction of joint inflammation; and total number of adverse events.

#### **Data Extraction and Synthesis**

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Two authors independently extracted data and assessed study trial suitability for inclusion. Risk of bias was independently assessed by 2 authors, conforming to the recommended methods of the Cochrane Collaboration. Disagreements were resolved by consensus. The authors pooled results with a random-effects model and calculated heterogeneity with I<sup>2</sup> statistics. Treatment effect was assessed with risk ratios for dichotomous outcomes and mean differences for continuous data and included 95% confidence intervals. To combine outcomes with different scales, standardized mean differences were calculated.

## **Results**

A total of 1,035 articles were identified with the search strategy, yet only 2 studies met the inclusion criteria (see table). The first study included 43 patients with acute gout, diagnosed by synovial analysis, and compared high-dose oral colchicine (1 mg initially followed by 0.5 mg every 2 hours until pain relief or adverse effects; mean total dose 6.7 mg) with placebo. Nonsteroidal anti-inflammatory medications were withheld from all patients for 48 hours. The second study included 575 patients with acute gout according to the American College of Rheumatology preliminary classification criteria who were randomized to one of 3 groups: high-dose oral colchicine (4.8 mg during 6 hours), low-dose oral colchicine (1.8 mg during 1 hour), or placebo. Nonsteroidal anti-inflammatory medications were allowed if patients had intolerable pain after the first dose of study drug. Patients' pain was recorded on continuous scales in both studies, whereas the first study also measured inflammation and the second study recorded adverse events.

## **Commentary**

Gout is a disease characterized by acute, severely painful attacks triggered by the deposition of monosodium urate crystals in joints. It is the most common cause of inflammatory arthritis in adults.<sup>1</sup> Multiple treatments have been used for acute gout flares, including nonsteroidal anti-inflammatory

medications, opioids, systemic corticosteroids, intra-articular corticosteroids, and ice<sup>1, 2, 3 and 4</sup>; however, the evidence behind many of these treatment modalities is limited. A recent systematic review found only 1 low-quality trial comparing nonsteroidal anti-inflammatory medications with placebo, which reported an increase in the proportion of patients with at least 50% pain reduction (risk ratio=2.75; 95% confidence interval 1.13 to 6.72).<sup>5</sup>

Colchicine is a medication that has been used for centuries in the treatment of inflammatory arthritis and acts by multiple mechanisms to suppress an acute gout flare.<sup>6</sup> However, significant concerns have been raised about the frequency of serious adverse effects from colchicine, particularly gastrointestinal distress, hematologic effects, acute kidney injury, and even death with excessive doses.<sup>6</sup>

The goal of this systematic review was to analyze the benefits and adverse effects of using colchicine to treat an acute gout flare. The authors conducted a rigorous search but were able to locate only 2 randomized controlled trials comparing colchicine to placebo and none comparing colchicine to other treatment modalities. The larger of the 2 trials was judged to be at uncertain risk of bias and was industry sponsored.<sup>7</sup> The other study was judged to be at low risk of bias but included only 45 patients.<sup>8</sup> Despite the limited data, colchicine appears to provide pain relief during acute gout flares at both high and low doses compared with placebo. The authors of this review calculated a number needed to treat of 4 for high-dose colchicine and 5 for low-dose colchicine. More important, the incidence of adverse effects, particularly gastrointestinal effects, was high, with a calculated number need to harm of 2 in the high-dose colchicine group; this low number highlights the high incidence of adverse events with colchicine.

Providers should weigh the risks and benefits of colchicine compared with other treatment options, considering the limited evidence for those alternative treatments as well. Research indicates that high-dose colchicine regimens are not superior, and they are not recommended by clinical guidelines. When

colchicine is used to treat an acute gout flare, a low-dose regimen (1.2 mg followed by a single 0.6-mg dose 1 hour later) appears to provide a similar benefit with less potential harm.

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Editor's Note: This is a clinical synopsis, a regular feature of the Annals' Systematic Review Snapshot (SRS) series. The source for this systematic review snapshot is: van Echteld I, Wechalekar MD, Schlesinger N, et al. Colchicine for acute gout. *Cochrane Database Syst Rev*. 2014;(8):CD006190.

**Table. Results for colchicine versus placebo in acute gout treatment.**

Colchicine	Outcome*	Placebo Risk	Colchicine Risk	Risk Ratio (95% CI)
High dose	50% or greater reduction in pain	240/1<comma>000	518/1<comma>000	2.16 (1.28–3.65)
50% or greater reduction in inflammation	48/1<comma>000	504/1<comma>000	10.50 (1.48–74.38)	3 (2–19)
Total adverse events	220/1<comma>000	838/1<comma>000	3.81 (2.28–6.38)	2 (2–5)
Low dose	50% or greater reduction in pain	172/1<comma>000	418/1<comma>000	2.43 (1.05–5.64)
Total adverse events	203/1<comma>000	257/1<comma>000	1.24 (0.55–2.79)	n/a†