



BRIEF ANSWERS  
TO SPECIFIC  
CLINICAL  
QUESTIONS

## Q: Should all patients with acute pericarditis be treated with colchicine?

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**A:** Colchicine should be considered a first-line treatment for acute pericarditis and for preventing recurrent episodes, in view of clinical evidence suggesting that it is superior to conventional therapy and has a relatively mild side-effect profile.

Colchicine has been used for centuries as an anti-inflammatory agent for acute gouty arthritis, but only within the last 2 decades has it been used in pericarditis, initially for recurrent pericarditis refractory to non-steroidal anti-inflammatory drugs (NSAIDs) or corticosteroids and recently in studies in patients with acute pericarditis as well.

Acute inflammation of the pericardium is most commonly idiopathic or viral, but it can also be caused by autoimmune mechanisms, uremia, or myocardial infarction.<sup>1</sup> Recurrent pericarditis is one of the most troubling and difficult-to-treat complications of acute pericarditis, occurring in 15% to 50% of cases.<sup>2</sup> Traditional treatments for recurrent pericarditis have included NSAIDs, corticosteroids, immunosuppressive agents, and pericardiectomy.

### ■ CLINICAL STUDIES OF COLCHICINE

#### In recurrent pericarditis

In 1987, Rodriguez de La Serna et al<sup>3</sup> proposed colchicine as a treatment for recurrent pericarditis, in view of its ability to prevent polyserositis in familial Mediterranean fever.

Only recently have larger and multicenter studies evaluated it in this role.

In a small, early, prospective study, Guindo et al<sup>4</sup> gave colchicine 1 mg/day to patients who had had at least three relapses of acute pericarditis while being treated with aspirin, indomethacin, prednisone, or a combination of these agents. No recurrence was observed in any patient during treatment with colchicine, and there was a significant difference between the symptom-free intervals before and after treatment with colchicine ( $3.33 \pm 4.3$  months vs  $24.3 \pm 16.1$  months,  $P < .002$ ).

Guindo et al<sup>5</sup> subsequently performed a larger prospective study in 51 patients with recurrent pericarditis, treating them with colchicine and following them for 6 to 128 months. All patients had been treated with NSAIDs, corticosteroids, pericardiocentesis, or a combination. Before starting colchicine, patients had a mean of  $3.58 \pm 3.64$  recurrences (range 2 to 15). During colchicine treatment, only 7 of the 51 patients had recurrences. In addition, the symptom-free period was significantly longer after starting colchicine treatment: 3.1 months vs 43 months.

Artom et al<sup>6</sup> analyzed 119 published and unpublished cases of patients treated with colchicine after at least two relapses of pericarditis. During follow-up ranging from 1 to 185 months, only 18% of patients had relapses while receiving colchicine treatment, and 30% had relapses after it was discontinued. The mean duration of colchicine treatment was  $24.5 \pm 23.3$  months in patients previously treated with corticosteroids and  $9.7 \pm 7.8$  months in patients not treated with corticosteroids.

**Recent studies support the use of colchicine for initial episodes of acute pericarditis and for preventing recurrences**

### In acute pericarditis

The Colchicine for Acute Pericarditis (COPE) trial,<sup>7</sup> the first, and to this date only, prospective randomized trial of colchicine for treatment of an initial episode of pericarditis, randomized patients to treatment with aspirin alone or aspirin with colchicine. Patients randomized to colchicine therapy were given 1 to 2 mg the first day and a maintenance dose of 0.5 to 1 mg daily for 3 months in addition to aspirin. Patients given colchicine in addition to aspirin had a more rapid resolution of symptoms, and fewer of them had recurrences (33.3% vs 11.7%,  $P = .009$ ).

### OUR RECOMMENDATIONS

In view of these data, we suggest that colchicine, given concurrently with aspirin or other NSAIDs, be considered as first-line therapy for patients presenting with acute pericarditis. Most patients can be started on 1 to 2 mg of colchicine the first day and then maintained on 0.5 to 1.0 mg daily. As colchicine is partially cleared by renal excretion, patients with renal insufficiency should receive a reduced dosage.<sup>8</sup>

Although there is no clearly defined length of colchicine therapy, the COPE trial investigators treated patients for 3 months, which we would recommend as a minimum. NSAIDs should be continued for approximately 4 weeks.<sup>7</sup> Patients who cannot tolerate NSAIDs can be given a trial of colchicine as monotherapy, which has been shown to be effective in several small studies.<sup>9,10</sup> Colchicine has been shown to be safe when given long-term, ie, 128 months.<sup>6</sup> Extended periods of treatment may be required in patients who have been treated with cortico-

steroids or who are corticosteroid-dependent.<sup>4</sup>

While gastrointestinal symptoms related to colchicine are not uncommon, they are generally not serious and resolve if the dose is reduced.<sup>7</sup> However, approximately 10% of patients may be unable to tolerate colchicine due to diarrhea (7% in the CORE trial<sup>11</sup>). Additionally, clinically significant interactions, including acute mononeuropathy, can occur when colchicine is combined with macrolide antibiotics, statins, and some calcium channel blockers.

### WHAT IS THE ROLE OF CORTICOSTEROIDS?

Some of the aforementioned studies<sup>2,6,7,11</sup> have confirmed that corticosteroid treatment is a risk factor for recurrent pericarditis. A possible mechanism is by permitting more viral replication, which would perpetuate pericardial inflammation.<sup>7</sup>

Physicians may worry that withholding corticosteroids in patients with repeated pericardial inflammation might increase the likelihood of constrictive pericarditis or pericardial tamponade. This is unlikely and has not been reported in clinical studies.<sup>12</sup> In fact, the clinical evolution of recurrent pericarditis is characterized by progressively less severe recurrences, usually without serious complications.<sup>2,13</sup>

Accordingly, we recommend that corticosteroids not be used for initial treatment of pericarditis or recurrences unless the patient has had no response to NSAIDs or colchicine or if these drugs are both contraindicated. ■

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We would give colchicine for at least 3 months in acute pericarditis