

Colchicine in acute pericarditis: why it remains underused

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Acute pericarditis, an inflammatory condition of the pericardium, often presents with debilitating chest pain and can lead to recurrent episodes, significantly impacting patient quality of life. While corticosteroids have long been a mainstay, their association with increased recurrence rates has driven the search for more effective and safer anti-inflammatory strategies. Colchicine has emerged as a critical adjunct, yet its integration into routine practice still lags behind the evidence.

KEY TAKEAWAYS

- **The Pivot:** Colchicine significantly reduces recurrence rates and improves symptom resolution in acute pericarditis.
- **The Data:** Clinical studies consistently show a benefit for colchicine in both initial and recurrent pericarditis.
- **The Action:** Clinicians should consider colchicine as a first-line adjunctive therapy in acute pericarditis, adhering to recommended dosing and duration.

Acute pericarditis is a common cause of chest pain, accounting for a notable proportion of emergency department visits for non-ischemic chest pain. The condition is characterized by inflammation of the pericardium, the sac surrounding the heart, often idiopathic but sometimes linked to viral infections, autoimmune diseases, or post-cardiac injury syndromes. Patients typically present with sharp, pleuritic chest pain, often relieved by leaning forward, and may have a pericardial friction rub on auscultation. Electrocardiogram changes, such as diffuse ST-segment elevation, and elevated inflammatory markers like C-reactive protein (CRP) are common diagnostic findings. The primary goal of treatment is to alleviate symptoms and prevent recurrence, a persistent challenge in managing this condition.

Standard initial therapy for acute pericarditis has historically involved non-steroidal anti-inflammatory drugs (NSAIDs) or aspirin, often combined with proton pump inhibitors to mitigate gastrointestinal side effects. Corticosteroids are reserved for specific indications, such as autoimmune etiologies or when NSAIDs are contraindicated or ineffective, due to their known association with increased rates of recurrent pericarditis. This recurrence, affecting up to 30% of patients after a first episode and up to 50% after a second, represents a significant unmet need, driving the exploration of therapies that can modulate the inflammatory response more effectively without promoting chronicity.

The Anti-Inflammatory Mechanism of Colchicine

Colchicine, an alkaloid derived from the autumn crocus, has a long history of use in inflammatory conditions, most notably gout. Its mechanism of action in pericarditis is primarily attributed to its anti-inflammatory and immunomodulatory effects. Colchicine disrupts microtubule formation, thereby inhibiting neutrophil chemotaxis,

adhesion, and activation. This interference with leukocyte migration and inflammatory mediator release reduces the inflammatory cascade within the pericardium. It also suppresses the inflammasome, a multiprotein complex that plays a critical role in the innate immune response and the production of pro-inflammatory cytokines like interleukin-1 beta (IL-1 β). This broad anti-inflammatory action makes colchicine particularly well-suited for managing the sterile inflammation characteristic of pericarditis.

The drug's efficacy in preventing recurrence is thought to stem from its ability to dampen the initial inflammatory insult more thoroughly, preventing the perpetuation of inflammation that can lead to chronic or recurrent disease. Its relatively rapid onset of action and oral bioavailability make it a practical option for both inpatient and outpatient management. But despite its clear mechanistic rationale and established clinical utility, the drug remains underutilized, often due to lingering misconceptions about its safety profile or a lack of familiarity with optimal dosing strategies.

Dosing and Duration: Getting it Right

Optimal dosing of colchicine in acute pericarditis is weight-adjusted and typically involves a loading dose followed by a maintenance dose. For patients weighing over 70 kg, the recommended regimen is often 0.5 mg twice daily, preceded by an initial loading dose of 0.5 mg three times daily on the first day. For those weighing 70 kg or less, the dose is typically 0.5 mg once daily, with a loading dose of 0.5 mg twice daily on day one. These dosages aim to achieve therapeutic concentrations while minimizing gastrointestinal side effects, which are the most common adverse events associated with colchicine.

The duration of colchicine therapy is equally important for preventing recurrence. Current guidelines generally recommend continuing colchicine for at least three months after a first episode of acute pericarditis, and for six months or longer in cases of recurrent pericarditis. This extended duration is important because premature discontinuation can lead to a rebound inflammatory response and subsequent recurrence. Gradual tapering of the dose, rather than abrupt cessation, is also often advised, though the evidence for tapering benefits is less robust than for extended duration. The management of chronic inflammatory conditions often requires such sustained approaches.

Clinical Evidence and Guideline Recommendations

Multiple randomized controlled trials have consistently demonstrated the benefit of colchicine in acute pericarditis. These studies have shown that adding colchicine to conventional anti-inflammatory therapy significantly reduces the rate of recurrent pericarditis, shortens the duration of symptoms, and improves the rate of complete symptom resolution. The effect is seen across various etiologies of pericarditis, including idiopathic, viral, and post-cardiotomy syndrome. The consistency of these findings has led major cardiology societies to issue strong recommendations for colchicine use. European guidelines, for instance, recommend colchicine as a first-line adjunctive therapy for both initial and recurrent acute pericarditis. These recommendations are based on high-level evidence, emphasizing the drug's role in improving clinical outcomes and reducing the burden of recurrent disease. Despite these clear directives, real-world data suggest that colchicine is not prescribed as frequently as it should be. This gap between evidence and practice is a persistent issue in many areas of medicine, and pericarditis management is no exception. Clinicians often find themselves navigating complex treatment algorithms, and sometimes, simpler, effective therapies are overlooked.

Safety Profile and Management of Side Effects

Colchicine is generally well-tolerated at the doses used for pericarditis, but side effects, primarily gastrointestinal, are common. Diarrhea, nausea, vomiting, and abdominal pain are the most frequently reported adverse events. These are typically dose-dependent and can often be managed by reducing the dose or temporarily interrupting treatment. Co-administration with food can also help mitigate gastrointestinal upset. Less common but more serious side effects include myopathy, rhabdomyolysis, and bone marrow suppression, particularly in patients with renal or hepatic impairment, or those taking interacting medications.

Drug interactions are a significant consideration. Colchicine is metabolized by cytochrome P450 3A4 (CYP3A4) and is a substrate of P-glycoprotein (P-gp). Therefore, co-administration with strong CYP3A4 inhibitors (e.g., clarithromycin, ketoconazole, diltiazem, verapamil) or P-gp inhibitors (e.g., cyclosporine, ranolazine) can significantly increase colchicine plasma concentrations, leading to toxicity. Careful medication reconciliation and dose adjustment are essential when prescribing colchicine, especially in polymorbid patients. For a comprehensive overview of drug interactions, clinicians may consult resources like the Oxford Handbook of Clinical Medicine.

Why the Underuse Persists

Several factors contribute to the underuse of colchicine in acute pericarditis. One major barrier is a lack of familiarity among some clinicians with the specific dosing and duration recommendations for pericarditis, often conflating it with gout treatment regimens. The historical perception of colchicine as a drug with a narrow therapeutic index and significant toxicity, largely based on older, higher-dose regimens for acute gout, may also contribute to reluctance. But the doses used for pericarditis are considerably lower and generally safer.

Another factor is the diagnostic challenge of pericarditis itself. Its symptoms can mimic other more serious cardiac conditions, leading to diagnostic delays or misdiagnoses. Once diagnosed, the focus often shifts to immediate symptom relief, sometimes overlooking the long-term strategy for recurrence prevention. The lack of readily available, condition-specific prescribing guidelines at the point of care can also be a barrier. Some clinicians may be hesitant to prescribe a drug for an extended period, particularly if the patient is asymptomatic, despite the clear evidence supporting prolonged therapy for recurrence prevention. This highlights a broader issue in medicine where adherence to guidelines for established therapies can be inconsistent.

Addressing the Gap in Practice

To improve the uptake of colchicine, educational initiatives are needed to inform clinicians about its established efficacy, appropriate dosing, and favorable safety profile at pericarditis-specific doses. Emphasizing the strong guideline recommendations and the long-term benefits in preventing recurrence can help overcome therapeutic inertia. Integrating colchicine into clinical pathways and electronic health record order sets for acute pericarditis could also streamline its use and ensure consistent application of evidence-based care. Patient education is also vital; informing patients about the rationale for prolonged therapy and potential side effects can improve adherence and reduce anxiety about long-term medication use. The goal is not merely to treat the acute episode, but to prevent the chronic, relapsing course that can severely diminish a patient's quality of life.

The open-label design of some earlier trials is an obvious caveat, but the consistency of findings across multiple studies, including more recent placebo-controlled designs, provides robust support for colchicine's efficacy. The trial populations have generally been representative of patients seen in clinical practice, but whether benefits extend equally to very

specific subgroups, such as those with severe renal impairment or specific autoimmune conditions, still warrants careful clinical judgment and individualized risk-benefit assessment. The long-term safety profile beyond six months, while generally good, also requires ongoing vigilance, particularly for drug interactions.

CLINICAL IMPLICATIONS

The evidence for colchicine in acute pericarditis is not merely suggestive; it is definitive. Clinicians who are not routinely incorporating colchicine into their management strategy for acute pericarditis are missing a clear opportunity to improve patient outcomes and reduce the burden of recurrent disease. The drug's ability to modulate inflammation without the recurrence-promoting effects of corticosteroids makes it an indispensable tool.

The persistent underuse points to a gap in knowledge dissemination or perhaps an ingrained conservatism in prescribing. The perceived risks, often extrapolated from higher-dose regimens for gout, overshadow the well-established safety profile at the lower, pericarditis-specific doses. This reluctance is costing patients unnecessary recurrences and prolonged suffering.

For patients, this means a higher likelihood of repeated hospital visits, ongoing pain, and the anxiety of unpredictable relapses. The simplicity of colchicine's oral administration and its relatively low cost should make it a readily accessible option, yet it often remains a second thought. It is time for a more proactive approach to its use, aligning practice with the robust evidence base.

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