Correspondence

Letter Regarding Article by Imazio et al, "Colchicine in Addition to Conventional Therapy for Acute Pericarditis"

To the Editor:

We congratulate Imazio et al[1] for their excellent article on colchicine in acute pericarditis. We see 2 take-home messages in this study: first, that colchicine is useful in the first attack, and second, that corticosteroid therapy given in the first attack favors the recurrence of pericarditis. This concept is in line with our recent findings that pretreatment with steroids attenuates the efficacy of colchicine in preventing recurrent pericarditis[2] and with animal experiments showing that corticosteroids may exacerbate virally induced pericardial injury. Thus, the results reported by Imazio et al[1] and those from our multicenter study should strongly encourage clinicians not to use corticosteroids except in extreme, very rare cases. Although their use may be very gratifying in the short term, it will greatly complicate the following course. On the other hand, a first episode of pericarditis is often treated with antibiotics, and coadministration of colchicine and macrolides may induce severe side effects,[3] so this drug combination should also be avoided.

Finally, Imazio et al excluded patients with current transaminase values >1.5 times the upper normal limit. In our cohort of 58 patients,[4] we observed 5 patients (8.6%) with abnormal liver test results in the first attack: 3 had alanine aminotransferase elevations ranging from 87 to 1100 U/L, and 2 had alkaline phosphatase elevations only, of 486 and 520 U/L. These abnormalities disappeared with resolution of the attacks. Therefore, we propose not to negate this potentially useful therapy in patients with abnormal liver test results. In the real world, colchicine should be used more and steroids much less often.

Disclosures

None.

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Response

We thank Drs Brucato, Adler, and Spodick for their interest and remarks on our article.[1] We agree with the main take-home messages.

However, caution should be recommended in the prescription of colchicine for acute pericarditis. At present, this use is unlabeled. The stronger evidence comes from a single, open-label, randomized study (the COlchicine for acute PEricarditis [COPE] trial). More evidence supports the use of colchicine in recurrences after failure of conventional treatment,[2] but the precise proportion of responders is not exactly known because appropriately randomized trials are lacking.[3] Nevertheless, colchicine was given a class IIa indication for acute pericarditis in the European guidelines.[4]

Although at low doses (0.5 to 1.2 mg/d) colchicine has been found to be safe even when given continuously over decades,[2] there are other less common (<1%) possible side effects to be considered (eg, bone marrow suppression, hepatotoxicity, and myotoxicity) beyond the well-known gastrointestinal side effects. Moderately increased liver enzyme values were observed in 7% of patients in the Marburg Pericarditis Registry.[5] Neuromyopathy with colchicine can occur even during long-term administration of therapeutic low doses. Chronic renal insufficiency leading to increased colchicine levels appears to be the major risk factor for this disorder and other possible negative interactions. Colchicine undergoes intensive hepatic metabolism (CYP 3A4). Consequently, drugs (cyclosporine, azole antifungals, ciprofloxacin, clarithromycin, diclofenac, doxycycline, erythromycin, isoniazid, nicardipine, propofol, protease inhibitors, quinidine, and verapamil) that interact with the cytochrome P-450 system may interfere with colchicine, thereby increasing the levels/effects of colchicine. Coadministration of colchicine and macrolides may also impair colchicine elimination by inhibition of P-glycoprotein, resulting in possible drug excess and toxicity, particularly in the elderly and/or the renally compromised.[6]

At present, it seems reasonable to avoid use of the drug in patients with hepatobiliary dysfunction, as well as those with severe renal, hepatic, and gastrointestinal disorders and blood dyscrasias. It is also prudent to reduce the maintenance/prophylactic dose by 50% in individuals >70 years of age and in patients with impaired renal function with glomerular filtration rates <50 mL/min. Although the safety profile of the drug seems to be superior to that of corticosteroids and other immunosuppressive drugs, every patient should undergo careful monitoring for possible side effects, including blood analyses (transaminases, serum creatinine, creatine kinase, and blood cell count).

In conclusion, although the findings of the COPE trial provide a stronger evidence base for the use of colchicine in acute pericarditis, they need to be confirmed in multicenter, possibly double-blind, randomized trials before routine use can be recommended.

Disclosures

None.

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