

Editorial

Is It Time for a “Reverse Paradigm Shift” in the Treatment of Acute Idiopathic Pericarditis?



¿Es hora de revertir el paradigma en el tratamiento de la pericarditis aguda idiopática?

Lovely Chhabra^{a,*} and David H. Spodick^b^a Department of Cardiology, Heartland Regional Medical Center, Marion, IL, United States^b Department of Medicine, Saint Vincent Hospital, Worcester, MA, United States

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We read with great interest the excellent work by Sambola et al. titled “Colchicine Administered in the First Episode of Acute Idiopathic Pericarditis: A Randomized Multicenter Open-label Study”, published in *Revista Española de Cardiología*, which investigated the role of colchicine in the first episode of acute idiopathic pericarditis.¹ There is one important conclusion and take-home message from the study: the addition of colchicine to conventional nonsteroidal anti-inflammatory drug (NSAID) treatment does not provide an added benefit in decreasing recurrences in patients with a first episode of acute idiopathic pericarditis (AIP) who had not previously received corticosteroids.

The routine use of colchicine in the treatment of a first episode of AIP began in clinical practice after the publication of the results of the randomized, open-label COPE study² and then similar findings were observed from the randomized, double-blind, placebo-controlled ICAP study.³ Based on the data from these studies, the European Society of Cardiology guidelines endorsed the use of colchicine for AIP as a class IA recommendation.⁴ The findings of Sambola et al. are, however, different from those of the COPE and ICAP studies. Some of the obvious differences in the findings of the current study could potentially be explained by the complete abstinence of corticosteroid use as a first-line therapy in treatment, the sole inclusion of idiopathic/presumably viral pericarditis (as opposed to other forms of pericarditis such as autoimmune or postpericardiotomy syndrome, etc.) and significantly lower observed rates of recurrence overall compared with the prior controlled investigations. The observed lower recurrence rates could partially be explained by the lack of the use of echocardiography to assess the interval change in pericardial effusion and also inflammatory markers in the current investigation.⁵ Changes in the effusion size and inflammatory markers may have potentially resulted in the inflation of recurrence rates by the prior investigations. One may argue that the interval change in the effusion size and change of inflammatory markers in the absence of the other 3 clinical markers of AIP (namely pericarditic chest pain, characteristic ECG changes, and pericardial rub)⁶ may only represent a subclinical recurrence and may not potentially alter the overall clinical outcome, as demonstrated in the current study.

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* Corresponding author: Heartland Regional Medical Center, 3331 W. DeYoung St, Marion, IL 62959, United States.

E-mail address: lovids@hotmail.com (L. Chhabra).

Regardless of the differences described in the observations between COPE, ICAP and the current study, one clear unifying message from all 3 randomized investigations is that the corticosteroid therapy given in the first attack favors the increased risk of disease recurrence. This is in line with our prior studies and hypothesis that pretreatment with steroids attenuates the efficacy of anti-inflammatory therapy and may permit viral replication, thus perpetuating pericardial injury.^{5,7} Thus, clinicians must strongly discourage the use of corticosteroids as a first-line therapy with some rare exceptions.⁸ These exceptions may include a clear underlying autoimmune trigger or connective tissue disease necessitating steroid use, uremia, contraindication to NSAID use, and/or suboptimal response to NSAID therapy.⁸ Although steroid use may often be successful in the short-term, it will greatly complicate the following course. If used for a rare indication, a very slow and gradual taper is recommended.⁸

An important question raised by the results of the CAFE-AIP study is: “Is it time for a change of current clinical treatment pattern for AIP (a reverse paradigm shift)?” In our opinion, we should carefully evaluate the results of all 3 studies and individualize appropriate clinical decision-making. We should also consider that it is not always easy to tease out acute idiopathic or viral pericarditis from other autoimmune forms due to an occasional overlap in the clinical spectrum.^{5,8} Colchicine helps to reduce recurrence rates, as shown by overwhelming evidence in the prior clinical trials including patients with both acute and recurrent pericarditis; however there was some mix of study population.^{9,10} The findings of the current trial provide a strong argument that the use of old conventional NSAID therapy alone is good enough, especially in patients with a first episode of AIP who have never been previously treated with steroids. These findings would offer even a stronger value if confirmed preferably in a larger multicenter, possibly double-blind, randomized trial enrolling only patients with a first episode of AIP and no prior steroid use. Regardless, if a patient has no autoimmune trigger and is otherwise determined to be a low-risk candidate, it may be reasonable to pursue treatment with NSAID therapy alone. Also, one may discourage the use of colchicine in patients with moderate-to-severe hepatobiliary dysfunction, severe chronic renal insufficiency, blood dyscrasias, and in those with use of some concomitant drugs (such as cyclosporine, azole antifungals, ciprofloxacin, doxycycline, macrolides, quinidine, and verapamil).¹¹

Although colchicine has been found to be potentially safe in the majority of patients in randomized studies, with gastrointestinal

upset being the most common adverse effect, there are other less common (< 1%) potential adverse effects to be considered (eg, bone marrow suppression, hepatotoxicity, myotoxicity, and neuromyopathy).¹¹ These potential adverse effects should be discussed with patients along with the potential benefits of colchicine use so that they can make a well-informed decision.

This study is a very important addition to the existing data on this subject. Future studies may potentially further strengthen our understanding of the role of colchicine. The role of colchicine in nonidiopathic forms of pericarditis also needs to be explored in future randomized investigations.^{12–14} Data from a randomized study in the United States would also be helpful. To date, the use of colchicine has not been approved by the Food and Drug Administration for pericarditis and remains an off-label indication.¹¹

In conclusion, we should definitely avoid the use of steroids in acute pericarditis as a first-line therapy, with rare exceptions as previously noted. NSAIDs and colchicine combination should be preferred to treat acute pericarditis in order to reduce the rate of future potential recurrence. In our opinion, based on the given data, the use of colchicine may be an option for patients who have a first episode of definite acute idiopathic or viral pericarditis, have never been previously treated with steroids, and demonstrate a good early clinical response to NSAIDs. In addition, well-informed decision-making among patients should be encouraged after a careful discussion of the potential benefits and adverse effects of pharmacotherapy options.

CONFLICTS OF INTEREST

D.H. Spodick receives honorarium from his textbook titled “The Pericardium: A Comprehensive Textbook (Fundamental and Clinical Cardiology)”.

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