The Efficacy of Colchicine in the Treatment of Recurrent Pericarditis Related to Postcardiac Injury (Postpericardiotomy and Postinfarcted) Syndrome: A Multicenter Analysis

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Abstract

\textbf{Background:} Pericarditis related to the postcardiac injury syndrome (PCIS) following myocardial infarction or cardiac surgery is a troublesome and often recurrent clinical entity resistant to therapeutic interventions. The usefulness of colchicine in the prevention of recurrent PCIS has not been evaluated. \textbf{Objective:} We performed a cumulative analysis of available multicenter data with the aim of evaluating the efficacy of colchicine in the treatment of recurrent PCIS. \textbf{Methods and Results:} The study was designed as a multicenter all-cases analysis. Researchers who had published studies and case reports on colchicine treatment in recurrent pericarditis related to PCIS during the last 15 years were approached and asked to contribute all available cases to the database. There were 28 patients, 18 male (64%) and 10 female (36%), ranging in age from 21 to 82 years (mean 53 ± 15 years). PCIS pericarditis was secondary to pericardiomy in 19 patients and infarction in 9. In 21 patients (75%), colchicine therapy was discontinued during follow-up and renewed only in the case of relapse. In these patients, the total period of treatment was summed up for analysis. 7 patients (25%) were taking colchicine as a permanent treatment, and no colchicine-free follow-up was documented. In total, 130 recurrences (mean 4.64 ± 3.7 per patient, range 2–16) were noted before colchicine therapy was initiated. During colchicine treatment (mean duration of treatment 16.6 ± 13.5 months), a significant reduction in the number of recurrences was observed. Only 5 of 28 patients (18%) presented with new recurrences (mean 0.25 ± 0.59 vs. 4.64 ± 3.7 per patient in the precolchicine period, \(p < 0.001\)). The mean follow-up period after colchicine discontinuation (data were available for 21 patients) was 31.9 ± 28 months; during follow-up, 13 patients (62%) remained recurrence free and 8 of them (38%) experienced relapses (mean 0.43 ± 0.6

Key Words

Pericarditis · Colchicine · Postcardiac injury syndrome · Postpericardiotomy syndrome · Postmyocardial infarction syndrome
per patient, \( p < 0.001 \) vs. precolchicine). **Conclusions:** It seems that colchicine may be effective in preventing new relapses in patients with recurrent pericarditis related to postcardiac injury both during active therapy and after its discontinuation.

### Introduction

Late pericarditis following myocardial infarction (Dressler’s syndrome) or cardiac surgery (Dressler’s-like syndrome) is referred to as postmyocardial infarction syndrome (PMIS) or postpericardiotomy syndrome, respectively [1, 2]. The term postcardiac injury syndrome (PCIS) is used to encompass both these entities [3, 4]. PCIS is characterized by fever, pleuropericardial pain, pericarditis and pulmonary involvement. Evidence supports an immunopathic etiology of this syndrome. Currently, the classical postmyocardial infarction Dressler’s syndrome has been rendered a rare phenomenon among patients who benefit from early revascularization [5]. In contrast, the incidence of postpericardiotoxic syndrome is high and varies from 13% [6] to 47% [7].

Postpericardiotoxic syndrome is a troublesome and often recurrent clinical entity [6–10]. Accepted modalities of PMIS treatment have traditionally included nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, immunosuppressive agents and, in unremitting cases, pericardectomy (usually unsuccessful), while relapses may occur during attempts to reduce drug dose. Unfortunately, recurrent pericarditis may be a debilitating disease resistant to therapeutic interventions [6–11].

Recently, the first study to demonstrate the benefits of colchicine for the primary prevention of postpericardiotoxic syndrome in patients after cardiac surgery was published [12]. However, the usefulness of colchicine in the prevention of recurrent PMIS has not been evaluated.

Therefore, we decided to perform a cumulative analysis of all available multicenter data in order to evaluate the efficacy of colchicine in treatment of recurrent PCIS.

### Methods

The study was designed as a multicenter all-cases analysis. Researchers who had published studies and case reports on colchicine treatment in recurrent pericarditis of any etiology during the last 15 years were approached and asked to contribute all available cases to the database. Patient data were obtained from Italy (\( n = 44 \)), Spain (\( n = 33 \)), France (\( n = 37 \)), Israel (\( n = 20 \)), Lebanon (\( n = 3 \)), Turkey (\( n = 2 \)) and Denmark (\( n = 1 \)).

A total of 140 cases were screened initially to investigate the following inclusion criteria:

1. PCIS etiology of pericarditis (postpericardiotoxic or postinfarction);
2. clinical diagnosis of two or more relapses of acute pericarditis before institution of colchicine therapy;
3. therapeutic trial of colchicine beyond its use during the tapering period of corticosteroids or NSAIDs;
4. complete documented follow-up since the first episode of acute pericarditis including reports on therapeutic trials with corticosteroids, and continuing for at least 1 month following initiation of colchicine therapy, and
5. colchicine dose of 1 mg/day for a prolonged period to achieve homogeneity of treatment.

In particular, data were considered complete only in patients with a methodical follow-up since the first episode of acute pericarditis, including precise information about the following predefined clinically relevant variables: age, sex, etiology of pericarditis, duration of follow-up since the first episode of pericarditis, use of corticosteroid therapy, number of relapses before initiation of colchicine treatment, duration of colchicine treatment and duration of follow-up after discontinuation of colchicine treatment. In addition, precise information needed to be documented about the number of relapses during colchicine treatment as well as during follow-up after discontinuation of colchicine treatment (postcolchicine). Twenty-one patients had to be excluded due to the lack of definitive age data or a colchicine dose different from 1 mg/day. In 91 patients, the etiology of pericarditis was other than PCIS (mainly idiopathic); these patients were also excluded. Therefore, the final study sample comprised 28 patients with PCIS pericarditis who met the inclusion criteria.

Results are expressed as mean values ± SD for continuous variables and as frequency and percentage for categorical variables. Comparison of categorical characteristics was performed by \( \chi^2 \) analysis and Fisher’s exact test. A t test was performed for continuous variables. A \( p \) value <0.05 was considered significant. Correlations between all continuous variables were conducted by Pearson correlation.

### Results

In this study, there were 28 patients, 18 male (64%) and 10 female (36%), ranging in age from 21 to 82 years (mean 53 ± 15 years). PCIS pericarditis was secondary to pericardiotoxicity in 19 patients and infarction in 9. In 21 patients (75%), colchicine therapy was discontinued during follow-up and renewed only in the case of relapse. In these patients, the total length of treatment was summed up for analysis. Seven patients (25%) were taking colchicine as a permanent treatment, and no colchicine-free follow-up was documented.

Despite treatment with NSAIDs, corticosteroids, pericardioticness or some combination thereof, all patients (100%) experienced relapses before inclusion in this study, representing statistics arising from the definition. In total, 130 recurrences (mean 4.64 ± 3.7 per patient,
**Table 1.** Follow-up duration and number of relapses in study patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before colchicine treatment</th>
<th>During active treatment with colchicine</th>
<th>Follow-up after colchicine treatment&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up duration, months</td>
<td>17.4 ± 29</td>
<td>16.6 ± 13.5</td>
<td>31.9 ± 28</td>
</tr>
<tr>
<td>Number of relapses per patient</td>
<td>4.64 ± 3.7</td>
<td>0.25 ± 0.59</td>
<td>0.43 ± 0.6</td>
</tr>
<tr>
<td>Number of patients with relapse</td>
<td>28 (100)</td>
<td>5 (18)</td>
<td>8 (38)</td>
</tr>
</tbody>
</table>

Figures in parentheses represent percentages.

<sup>1</sup> Available for only 21 patients.

**Table 2.** Pearson correlation coefficients between duration of follow-up, number of relapses and age of patients with PCIS

<table>
<thead>
<tr>
<th>Age</th>
<th>Follow-up before</th>
<th>Number of relapses before</th>
<th>Duration of treatment</th>
<th>Number of relapses during</th>
<th>Follow-up after</th>
<th>Number of relapses after</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.0</td>
<td>-0.46*</td>
<td>-0.48*</td>
<td>-0.13</td>
<td>-0.17</td>
<td>-0.21</td>
</tr>
<tr>
<td>Follow-up before</td>
<td>1.0</td>
<td>0.49*</td>
<td>-0.10</td>
<td>-0.16</td>
<td>-0.12</td>
<td>0.16</td>
</tr>
<tr>
<td>Number of relapses before</td>
<td>1.0</td>
<td>0.07</td>
<td>-0.13</td>
<td>0.13</td>
<td>0.05</td>
<td>0.52*</td>
</tr>
<tr>
<td>Duration of treatment</td>
<td>1.0</td>
<td>0.32</td>
<td>-0.35</td>
<td>0.25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of relapses during</td>
<td>1.0</td>
<td>-0.23</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up after</td>
<td>1.0</td>
<td>-0.34</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of relapses after</td>
<td>1.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

‘Before’, ‘during’ and ‘after’ refer to the periods before, during and after colchicine treatment. * p < 0.05.

**Discussion**

Colchicine has traditionally been used for the treatment of gout. The complex actions of this substance, which are mainly attributable to its stabilizing action on the cytoskeleton and cell membranes, and its special pattern of distribution form the basis for the results presented here regarding the prophylactic or therapeutic actions of colchicine in a whole range of other diseases. This is all the more significant in that in several instances it concerns diseases that have so far been unsatisfactorily con-
controlled by other treatments [13]. The present multicenter analysis demonstrates that colchicine is effective in preventing recurrences of pericarditis in PCIS. These results are especially important, since the study included patients with a high risk of recurrence (on average, more than 4 previous relapses per patient).

Considering the natural course of the disease, which is characterized by periodical relapses [14], it might have been expected that patients would experience new recurrences after discontinuation of therapy. However, during a mean follow-up period of more than 2 years, 62% of the patients in whom colchicine was discontinued remained free from new relapses. The absence of a correlation between the numbers of relapses per patient in the different periods of follow-up (before, during and after colchicine) indeed supports the concept that colchicine therapy provides sustained benefit even after discontinuation of the drug.

**Study Limitations**

The present study is an analysis of patients with recurrent PCIS with substantial variation in the number of previous relapses and the timing of instituting colchicine therapy as well as treatment duration. Eventually, only a randomized placebo-controlled double-blind trial may provide a definitive conclusion regarding optimal therapy for recurrent PCIS. However, in the absence of these data, the analysis of the present database provides an important source of information to guide the treatment of this problematic patient group.

**Conclusions**

It seems that colchicine may be effective in preventing new relapses in patients with recurrent pericarditis related to postcardiac injury both during active therapy and after its discontinuation.

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**References**