Journal of Clinical Pharmacology and Therapeutics

ISSN: 2766-8347

Case Report

Successful Rapid Desensitization to Colchicine in A 30-Year-Old Woman with Recurrent Pericarditis

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Abstract

Colchicine is an anti-inflammatory drug essential for treating recurrent pericarditis, gout, and familial Medi-terranean fever. Despite its benefits, hypersensitivity reactions, such as urticaria and angioedema, can limit its use, posing a significant challenge in managing conditions like pericarditis. Desensitization protocols may enable patients with hypersensitivity to safely resume colchicine therapy.

A 30-year-old woman with recurrent pericarditis developed a hypersensitivity reaction, including urticaria and angioedema, shortly after starting colchicine, leading to treatment discontinuation. Following a pericarditis relapse, an allergology work-up and an oral desensitization protocol for colchicine were performed using 3 dilutions and 9 steps, reaching a cumulative dose of 1 mg.

The patient successfully completed the oral desensitization protocol without hypersensitivity reactions and resumed colchicine at 0.5 mg/day. In the subsequent days, the colchicine dose was gradually increased to 1 mg/day with no further allergic reactions.

This case is the first to demonstrate successful oral desensitization to colchicine in a patient who developed an allergic reaction. Desensitization allowed the safe reintroduction of colchicine, indicating its potential as a treatment strategy. Standardized protocols could aid clinicians in managing similar cases, ensuring continued access to this therapy.

Introduction

Colchicine is an anti-inflammatory drug commonly used to treat and prevent conditions such as pericarditis, gout, and familial Mediterranean fever. It works by inhibiting microtubule polymerization, which in turn disrupts the migration of neutrophils to inflamed areas. This mechanism reduces inflammation, making colchicine a cornerstone in managing recurrent pericarditis, often in combination with other anti-inflammatory medications [1].

Despite its therapeutic benefits, colchicine can cause adverse reactions, including gastrointestinal symptoms such as diarrhea and nausea, but in rare cases hypersensitivity reactions such as urticaria and angioedema [2,3]. Potential mechanisms of allergy to colchicine may include IgE-mediated or non-IgE-mediated immune response (cytokine release and complement activation reactions). A useful method to unveil the IgE-mediated nature of hypersensitivity reaction is represented by a positive skin test with the culprit drug. Nevertheless, skin tests for colchicine are not standardized.

Allergy to colchicine is particularly challenging because alternative treatment options for conditions like recurrent pericarditis are limited. Thus, in such cases, desensitization protocols could provide a valid method to induce immune tolerance to the culprit drug, allowing patients to resume therapy without experiencing allergic reactions [4].

Desensitization protocols are widely used for drugs like antibiotics, aspirin, chemotherapeutics and recombinant enzymes, and it can be performed intravenously, subcutaneously or orally depending on the administration route of the drug in question [5-9]. This procedure is indicated when type-I hypersensitivity reactions occur; it is not recommended in patients who experienced life-threatening immunocytotoxic reactions or severe cutaneous reactions because of the potential life-threatening nature of these events [4].

The general rule is that the drug should be diluted several times to reduce the concentration, and administration should be started from the lowest concentration. The administered dose should be doubled every 15-20 minutes until the pre-established target dose is reached. The mechanism underlying desensitization is still under study, but evidence showed that increasing sub-therapeutics doses of the drug lead to mast cell and basophil unresponsiveness [4,10].

In this study, we present the first case of successful desensitization to colchicine in a patient with recurrent pericarditis and a documented hypersensitivity reaction to the drug.

Citation: Spataro F, Desantis V, Di Girolamo A, Ria R, Vacca A, Solimando AG. Successful Rapid Desensitization to Colchicine in A 30-Year-Old Woman with Recurrent Pericarditis. J Clin Pharmacol Ther. 2025;6(1):1065.

Publisher Name: Medtext Publications LLC

Manuscript compiled: Jan 06th, 2025

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Methods

Case Presentation

In May 2024, a 30-year-old non-atopic woman presented to the emergency department at Mater Dei Hospital, Bari, with chest pain and dyspnea. She was admitted to the Cardiology Department, where pericarditis with pericardial effusion was diagnosed. Colchicine therapy was initiated as part of the standard treatment. However, within 10 minutes of taking the first dose, the patient developed a generalized urticarial rash and face angioedema as shown in Figure 1 (grade 1 reaction according to World Allergy Organization anaphylaxis guidance, 2020) [11]. The allergic reaction resolved after approximately 72 hours with intramuscular antihistamines and intravenous corticosteroids. Following this episode, colchicine was discontinued, and the patient was treated with aspirin and corticosteroids orally. Over the next few months, the patient showed little improvement with this alternative therapy. No history of chronic spontaneous urticaria is reported.

However, in September 2024, she was admitted to the "G. Baccelli" Internal Medicine Department at Policlinico Hospital in Bari due to pericarditis relapse. Given the critical role of colchicine in managing this condition, the decision was made to reintroduce the drug at an initial dose of 0.5 mg/day. Thus, given the need to reintroduce colchicine, the allergic reaction manifested and the urgency to proceed, an allergology work-up and subsequent oral desensitization to colchicine were conducted.

Figure 1: Face angioedema after Colchicine assumption.

Skin testing

A skin prick test using colchicine 1 mg, diluted in 1 ml of saline solution (1 mg/ml), was performed to assess the possibility of an IgE-mediated hypersensitivity reaction. Skin prick test with histamine (10 mg/ml) and saline solution were used as the positive and the negative controls, respectively. The skin prick test is deemed positive when a wheal ≥ 3 mm larger than the negative control occurs [12].

Desensitization protocol

Given the need to reintroduce colchicine, an oral desensitization protocol was implemented. It consisted in 3 dilutions and 9 steps. The target dose was 1 mg.

The following dilutions were prepared:

- Mother solution: 2 tablet of colchicine 1 mg in 100 ml of water (0.02 mg/ml).
- Solution A: 10 ml of the mother solution in 90 ml of water (0.002 mg/ml).
- Solution B: 10 ml of solution A in 90 ml of water (0.0002 mg/ml).

The protocol begins with the solution B and continues the subsequent steps of the solution A and mother solution. No premedication was administered. The desensitization procedure had 9 sequential steps with increasing dosages at each dilution. Each dose was administered every 15 minutes. The whole procedure lasted 2 hours. The procedure is reported in Table 1.

The total cumulative dose administered was 1.039 mg of colchicine.

Table 1: Oral desensitization protocol for colchicine. Target dose: 1 mg.

STEP	SOLUTION	TIME (MIN)	VOLUME (ML)	DOSE (MG)
1	B	0	5	0.001
2	B	15	15	0.003
3	B	30	30	0.006
4	A	45	5	0.01
5	A	60	15	0.03
6	A	75	45	0.09
7	Mother	90	10	0.2
8	Mother	105	15	0.3
9	Mother	120	20	0.4
TOTAL				1.039

Dilutions:

Mother solution: 2 tablet of colchicine 1 mg in 100 ml of water (0.02 mg/ml).

Solution A: 10 ml of the mother solution in 90 ml of water (0.002 mg/ml).

Solution B: 10 ml of solution A in 90 ml of water (0.0002 mg/ml).

Results

Skin test result

The skin prick test for colchicine was negative, indicating no IgE-mediated type hypersensitivity reaction. The skin test with saline showed no reaction, while histamine skin test resulted in a wheal with a mean diameter of 4 mm.

Desensitization result

The desensitization protocol was successfully completed without any allergic reactions or adverse effects. On the day following desensitization, the patient was started on 0.5 mg/day of colchicine, administered as 0.25 mg twice daily. Four days later, colchicine was increased to 1 mg/day.

To date, the patient has tolerated colchicine without further hypersensitivity reactions.

Discussion

Colchicine is an essential drug in the management of recurrent pericarditis due to its anti-inflammatory effects. However, hypersensitivity to colchicine, although rare, poses a significant treatment challenge leading to drug discontinuation. Thus, an allergy work-up and desensitization procedure must be considered. Evidence about drug desensitization efficacy is obtained from antibiotics, aspirin, chemotherapy, recombinant enzymes and monoclonal antibody.

This case report is the first to our knowledge on colchicine desensitization in a 30-year-old woman affected by recurrent pericarditis. She experienced a significant immediate hypersensitivity reaction characterized by face angioedema and generalized urticaria 10 minutes after colchicine tablet assumption. Given the need to

reintroduce colchicine for relapse of pericarditis and the immediate nature of the hypersensitivity reaction, an allergy work-up for colchicine was performed. The skin prick test deemed negative, suggesting no IgE-mediated reaction. This suggests that mechanisms other than specific IgE-mediated pathway could be in-volved, such as direct basophils/mast cells by the drug, involvement MRXGPRX2 receptor, or complement activation with anaphylatoxins (C3a, C5a) production and subsequent mast cell/ basophil activation [4]. In these cases, skin tests could be negative, as for taxane or recombinant enzymes allergy where immediate reactions are often not IgE-mediated and skin tests are negative [8,13]. However, desensitization for these drugs is effective and safe. Thus, an oral 3-dilution, 9-step desensitization protocol for colchicine was implemented and performed. The patients tolerated the procedure without adverse events. The successful outcome of this procedure demonstrates its potential to safely reintroduce colchicine in similar cases. In Figure 2, we present the administration curve of colchicine, illustrating a gradual increase in dosage. The protocol begins with a very low initial dose, which is then progressively escalated through subsequent steps until reaching the target dose. The curve exhibits an exponential pattern, as each step involves doubling or even tripling the previous dose. Notably, one hour after the start of administration, the patient's cumulative dose remained approximately 20 times below the target dose. This slow escalation, with subtherapeutic dosing, is necessary to allow time for mast cells and basophils to enter a state of non-responsiveness, minimizing the risk of adverse reactions.

Further research is needed to develop standardized protocols for both skin testing and desensitization for colchicine. In this case, the negative skin prick test, combined with successful desensitization, suggests that IgE-mediated reactions may not be the predominant mechanism in colchicine hypersensitivity, but more studies and laboratory tests are required to confirm this hypothesis.

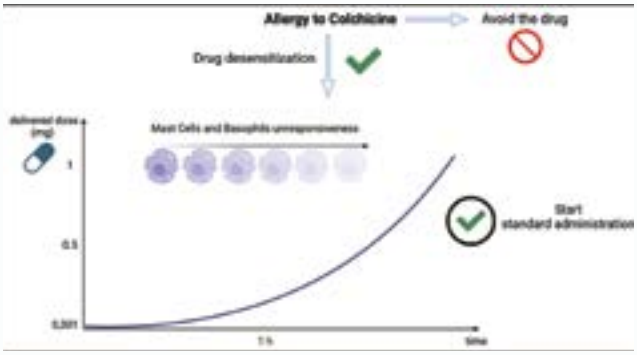

Figure 2: Colchicine desensitization curve.
h: hours

Conclusion

This case report describes the first successful desensitization to colchicine in a patient with recurrent pericarditis and hypersensitivity to the drug. The desensitization protocol allowed the patient to resume colchicine therapy without further allergic reactions, highlighting its potential role in managing colchicine hypersensitivity. Further research is necessary to establish standardized protocols for both skin testing and desensitization to colchicine, thus providing a framework for safely managing patients with similar hypersensitivity profiles.

Funding and Acknowledgement

This study was funded by the Complementary National Plan PNC-I.1 "Research initiatives for innovative technologies and pathways in the health and welfare sector" D.D. 931 of 06/06/2022, DARE - DigitAl lifelong pRevEntion initiative, code PNC0000002, CUP B53C22006420001, by the Italian network of excellence for advanced diagnosis (INNOVA), Ministero della Salute -code PNC-E3-2022-23683266 PNC-HLS-DA, CUP: C43C22001630001 for the support. This research was also supported by the postgraduate school of Allergy and Clinical Immunology Program, Bari Aldo Moro University.

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