

Clinical Communications

Thiocolchicoside: An unusual suspect of drug hypersensitivity

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Clinical Implications

- Thiocolchicoside is commonly used as a muscle relaxant and it is underestimated as a cause of immediate hypersensitivity. This is the first study to report immediate reactions to thiocolchicoside with positive intradermal test results validated by negative test results in exposed controls.

TO THE EDITOR:

Thiocolchicoside is a natural derivative of colchicine and a semisynthetic derivative of the naturally occurring colchicoside extracted from the seeds of *Gloriosa superba* (*Liliaceae*). Thiocolchicoside exhibits a selective affinity for the inhibitory gamma-aminobutyric acid and glycinergic receptors. It has an agonistic action at the spinal-strychnine-sensitive receptors that can mediate its myorelaxant effect.¹ Because it is less sedating than other centrally acting muscle relaxants and has anti-inflammatory and analgesic actions, thiocolchicoside is commonly used in the treatment of acute muscle spasms and contractures and also in chronic osteoarticular, rheumatic, and neurologic disorders.^{1,2}

Peak plasma concentrations of the drug are achieved after 30 or 50 minutes, when administered intramuscularly or orally, respectively, and the molecule half-life is 4.5 hours.¹ It has a proconvulsant action and hence should be avoided in patients predisposed to seizures. Additional known side effects include other central nervous system and psychiatric events.³

Cases of anaphylactic reactions, urticaria, and angioedema as hypersensitivity manifestations following intramuscular injection are uncommon.³ However, a few cases of *Embolia cutis medicamentosa* (or Nicolau syndrome) after thiocolchicoside administration are described in the literature.⁴ Nicolau syndrome consists in the occurrence of immediate excruciating pain, early pallor, erythema, and edema at the injection site, followed by cutaneous, subcutaneous, or even muscular aseptic necrosis with a livedoid pattern.⁴

Furthermore, delayed hypersensitivity reactions such as contact dermatitis and photosensitivity reactions have been reported following thiocolchicoside injection.²⁻⁴

Only 2 cases of immediate allergic reaction to thiocolchicoside were found in the literature and both had documentation of positive skin prick test (SPT) results.^{5,6} Currently, there are no validated concentrations for intradermal tests (IDTs) with thiocolchicoside in allergy diagnosis.

We describe the case of a 56-year-old woman who reported generalized pruritus, palmar and plantar erythema, dyspnea,

wheezing and abdominal cramps (grade 3 anaphylaxis—Mueller), 5 minutes after intramuscular (IM) administration of thiocolchicoside and diclofenac. These symptoms promptly reverted after IM adrenaline (0.3 mg) and intravenous hydrocortisone (200 mg). Blood sample collected during the anaphylactic episode (30 minutes after symptoms) revealed an increase in serum tryptase (47 µg/L) and basal serum tryptase level was 4.3 µg/L ($N < 11$ µg/L). This woman reported previous exposure to diclofenac and thiocolchicoside with tolerability.

SPT (25 mg/mL), IDT (0.025-25 mg/mL) with diclofenac (75 mg/3 mL; Voltaren, Novartis Pharma, Basel, Switzerland), and the oral challenge (cumulative dose 100 mg) were negative, excluding diclofenac as culprit.

The skin tests were performed with thiocolchicoside (4 mg/2 mL; Relmus, Sanofi-Aventis, Paris, France) with sodium chloride as the only excipient. The SPT (2 mg/mL) and the IDT (0.02-0.2 mg/mL) results were negative, but 5 minutes after performing IDT (2 mg/mL), the patient complained of throat tightness, laryngeal dyspnea and pruritus in the tested arm, and presented a flare in the IDT (2 mg/mL) baseline bleb, soft palate edema, and oropharyngeal hyperemia, which resolved with oral ebastine 20 mg and prednisolone 40 mg in less than 1 hour.

We report a second case of a 52-year-old man who experienced dizziness, malaise, and hypotension (systolic blood pressure < 90 mm Hg) (grade 4 anaphylaxis—Mueller) 40 minutes after IM administration of thiocolchicoside and diclofenac. Treatment included volume expansion with saline, and intravenous hydrocortisone; no adrenaline was administered. The basal serum tryptase was 3.7 µg/L ($N < 11$ µg/L). This man also reported previous exposure to diclofenac and thiocolchicoside with tolerability. SPT (25 mg/mL), IDT (0.025-25 mg/mL) (75 mg/3 mL; Voltaren), and oral challenge with diclofenac (cumulative dose 100 mg) were negative, as in the first case. SPT (2 mg/mL) and IDT (0.02-0.2 mg/mL) with thiocolchicoside were negative, and IDT (2 mg/mL), with 3 mm mean diameter of induced bleb, was positive with 10 mm mean wheal diameter, at 20 minutes reading.

The SPT (2 mg/mL) and IDT (0.02-2 mg/mL) were performed to 6 patients with suspected immediate reaction to thiocolchicoside and were negative in all subjects, hence excluding an irritative reaction to the IDT with the higher concentration (2 mg/mL) of this molecule. Nonetheless, these patients also underwent negative drug provocation test with thiocolchicoside, confirming the negative result of skin tests.

A drug provocation test with thiocolchicoside was not performed in the 2 reported study cases because of severity of the index reactions (grade 3 and grade 4 anaphylaxis—Mueller).

This study is relevant because it supports the diagnosis of an IgE-mediated mechanism of hypersensitivity to thiocolchicoside based on intradermal tests in patients with immediate reactions to thiocolchicoside, validated by negative drug challenges in patients with negative skin test results. Moreover, because it is often prescribed concomitantly with nonsteroidal anti-inflammatory drugs, which is a common cause of drug hypersensitivity, it is probably underestimated as a cause of immediate hypersensitivity and highlights the importance of exploring all the coadministered drugs in allergy investigation.

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