

Immediate rhinoconjunctivitis induced by metamizole and metronidazole

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Objective: To report a case of immediate rhinoconjunctivitis induced by both metamizole and metronidazole.

Methods: Skin-tests (prick and intradermal) were performed with metamizole, metronidazole, and espyramicine. Standard RAST was carried out with metamizole and metronidazole. Oral challenge tests were performed single blind with Rhodogil, metronidazole, espyramicine, metamizole, aspirin, and propyfenazone.

Results: Both skin tests and RAST were negative. We also found that the patient tolerated therapeutic doses of espyramicine, aspirin, and propyfenazone. Challenges with Rhodogil, metamizole, and metronidazole elicited immediate rhinoconjunctivitis.

Conclusion: This is an exceptional case of immediate rhinoconjunctivitis induced by two unrelated drugs (metamizole and metronidazole). The pathogenic mechanism implicated in this process remains unclear. Inhibition of the cyclooxygenase pathway was excluded and we could not demonstrate the presence of specific IgE antibodies. Nevertheless, an immunologic or idiosyncratic mechanism could be responsible.

Ann Allergy Asthma Immunol 1997;78:345-6.

INTRODUCTION

Metamizole is the sodium sulfonate derived from aminopyrine (Fig 1), a pyrazolone nonsteroidal antiinflammatory agent used in our country. Pharmacologic actions are similar to aspirin which is able to inhibit the cyclooxygenase pathway. This drug produces a relatively high incidence of allergy and intolerance. Urticaria, anaphylaxis and asthma are the most frequently reported reactions.^{1,2}

Metronidazole, a nitroimidazole (Fig 1), is an antiprotozoal agent generally well tolerated, despite its widespread use. Cutaneous reactions, serum sickness, and systemic hypersensitivity reactions have been reported rarely.³⁻⁵

We report the case of a patient who presented an exceptional clinical reaction consisting of immediate rhinoconjunctivitis following administration of

two different drugs, metamizole and metronidazole.

CASE REPORT

The patient is a 19-year-old woman with history of facial angioedema and rhinoconjunctivitis due to horse hair sensitization. One year prior to her first visit to our department, she had been treated with Nolotil (575 mg metamizole) for a toothache; 15 minutes after the first dose, she experienced nasal and ocular itching, rhinorrhea, sneezing, and watery eyes. There was no shortness of breath, wheezing or cutaneous symptoms. Antihistamines were administered through an emergency service and the reaction was controlled within one hour.

Six months later, for the same problem, the patient received two tablets of Rhodogil (750,000 IU espyramicine and 125 mg metronidazole); 15 minutes after the first dose she developed a reaction similar to that described above.

She had previously tolerated both drugs and there was not any other apparent precipitating factor.

She had no clinical history of nasal polyps, chronic rhinitis, sinusitis, nor asthma. She had received aspirin before and after both reactions without any problem.

Physical examination was normal. The skin prick tests to common inhalants (mites, pollens, molds, and dander) were all negative but horse hair extract elicited a positive cutaneous response. Total serum IgE (CAP System) was 502 KU/L. Serum specific-IgE to horse hair (CAP-System) was 0.87 KU/L.

Skin tests (prick and intradermal) with metamizole, metronidazole, and espyramicine diluted in saline were negative. A specific-IgE analysis carried out by standard RAST was also negative for metamizole and metronidazole.

Oral drug challenges with metamizole, Rhodogil, espyramicine, metronidazole, aspirin, and propyfenazone were performed single-blind after obtaining written informed consent. Only one drug was administered each day. After a positive reaction, the next challenge was separated by at least 2 weeks. Progressively increasing doses, with 1-hour intervals, were given until reaching the therapeutic dose or the appearance of clinical symptoms.

Ten minutes after 150 mg metamizole, the patient developed intense rhinoconjunctivitis; at that moment, the pulmonary auscultation was normal and no changes were observed in FEV₁ values and blood pressure readings. Dexchlorpheniramine was administered and the symptoms subsided within one hour.

On another day, ten minutes after the administration of one tablet of Rhodogil (750,000 IU espyramicine and 125 mg metronidazole) the patient had the same reaction as described

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Received for publication June 12, 1996.

Accepted for publication in revised form November 29, 1996.

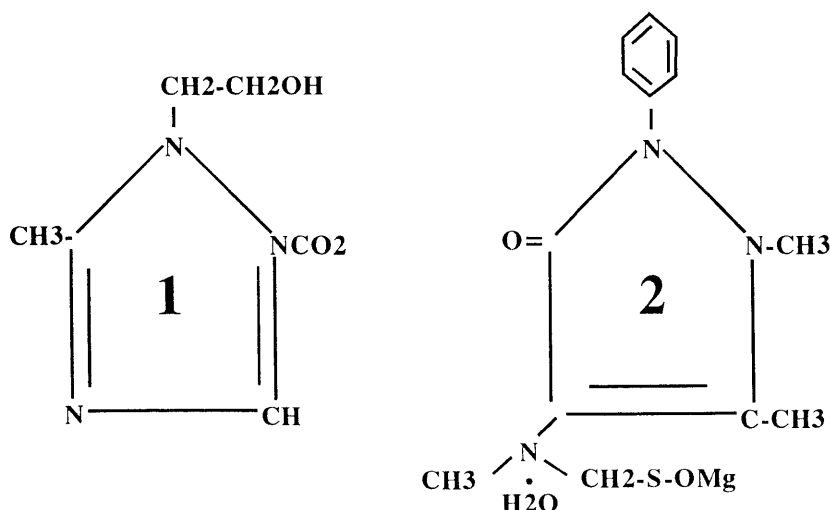


Figure 1. Chemical structure of metronidazole (1) and metamizole (2).

above for metamizole. Later, we undertook challenge with the different compounds of Rhodogil (espyramicine and metronidazole) separately. Thirty minutes after 75 mg metronidazole (Flagyl) she developed another episode of rhinoconjunctivitis.

Afterwards the patient tolerated 1.5 million units of espyramicine (Rovamicine) and therapeutic doses of aspirin and propyphenazone without any reactions.

A control patient, with immediate urticaria and skin prick test positive to metamizole, underwent oral challenge with 250 mg metronidazole with a negative result.

DISCUSSION

We report an exceptional case of immediate rhinoconjunctivitis induced by two different drugs (metamizole and metronidazole) in an atopic woman, as demonstrated by oral challenges.

There are two major types of adverse reactions to pyrazolone, allergy and intolerance. The allergic patients

are more often atopic women with elevated serum IgE levels and good tolerance to other aspirin-like drugs.¹ Patients with intolerance to the drug usually have asthma, chronic rhinitis, nasal polyps, and sensitivity to aspirin and other cyclooxygenase inhibitors.^{1,2} The mechanism involved in the reaction of our patient remains unclear. Inhibition of the cyclooxygenase pathway was excluded due to good tolerance of aspirin and other nonsteroidal anti-inflammatory drugs. Symptoms are consistent with, or even suggestive of an underlying allergic etiology, but the role of IgE as a mediating agent could not be demonstrated. We could therefore not elucidate the true mechanism involved. Other immunologic or idiosyncratic mechanisms cannot be ruled out in this process because additional diagnostic study was not possible.

Metronidazole is generally well tolerated. There have been isolated reports of immediate allergic reactions including urticaria, rash, or broncho-

spasm to this drug.²⁻⁵ To date and to best of our knowledge, the case reported here is the first case described of immediate rhinoconjunctivitis due to metronidazole.

Our patient had acute rhinoconjunctivitis induced by two unrelated drugs, metamizole and metronidazole. This could be due to a multiple drug hypersensitivity or to the presence of a common epitope to both drugs (Fig 1). In this case, the epitope would be different from the antigenic determinant responsible of pyrazolone allergy in other patients since the control patient with demonstrated metamizole allergy tolerated metronidazole.

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