

- 1) chronic pruritus may be induced by food additives
- 2) this kind of food-additive intolerance seems to be associated specifically with sodium nitrate
- 3) chronic generalized pruritus caused by food-additive intolerance might be more common than generally believed.

Acknowledgments: I thank the nurses of the allergy center – Stefania Arienti, Ombretta Dolcino, and Aurelio Tirloni – for their cooperation in carrying out double-blind challenges.

Ambulatorio di Allergologia
Ospedale Caduti Bollatesi
Via Piave 20
20021 Bollate (MI)
Italy

Accepted for publication 17 March 2000
Allergy 2000; 55:678–679
Copyright © Munksgaard 2000
ISSN 0105-4538

References

1. ASERO R. Chronic generalized pruritus caused by nitrate intolerance. *J Allergy Clin Immunol* 1999;**104**:1110–1111.
2. GREAVES MW. Chronic urticaria. *N Eng J Med* 1995;**332**:1767–1772.
3. SIMON RA, STEVENSON DD. Adverse reactions to food and drug additives. In: MIDDLETON E, REED CE, ELLIS EF, ADKINSON NF, YUNGINGER JW, BUSSE WW, editors. *Allergy: principles and practice*. 4th ed. St Louis, MO: Mosby, 1993:1687–1704.

Hypersensitivity to H₁-antihistamines

P. Demoly*, D. Messaad, S. Benahmed, H. Sahla, J. Bousquet

Key words: drug hypersensitivity; H₁-antihistamines.

- H₁-ANTIHISTAMINES are widely used antiallergic drugs. Hypersensitivity

reactions to H₁-antihistamines have been rare since the 1940s (1–5). We report the case of a patient with skin reactions to some, but not all, antihistamines, as demonstrated by oral challenges.

A 57-year-old woman consulted her general practitioner for scalp itching and erythematous eruption the day after she her hair dyed. She was first given dexchlorpheniramine 2 mg. Hydroxyzine 50 mg and betamethasone 0.25 mg were added 2 days later because of the persistence of the symptoms. Four hours after the first tablets, she experienced generalized urticaria, which persisted for 5 days on methylprednisolone 60 mg and hydroxyzine 100 mg daily, and disappeared after another 3 days on methylprednisolone alone (hydroxyzine having been stopped because of sleepiness). No etiology was looked at. A vague and mild itching sensation had persisted since that time. A month later, she took cetirizine 10 mg for an exacerbation of her itching and developed generalized urticaria after 2 h. She recalled a similar episode 7 or 8 years before with an composite medication for influenza containing triprolidine. She had no other medical history apart from persistent rhinosinusitis.

Four months after the initial symptoms, the patient underwent skin prick tests to codeine phosphate 9%, histamine phosphate 10 mg/ml (positive controls), dexchlorpheniramine 5 mg/ml, hydroxyzine 50 mg/ml, and the most common aeroallergens of our area. She also underwent patch tests with dexchlorpheniramine, hydroxyzine (5% in petrolatum), and the European standard series. The patient refused challenges to dexchlorpheniramine and hydroxyzine, which produced the most awkward reaction.

A rare case of skin reactions to dexchlorpheniramine and hydroxyzine.

Single-blind, placebo-controlled challenges with cetirizine, loratadine, mequitazine, fexofenadine, mizolastine, and cimetidine were performed. Increasing doses (starting with 0.1 mg) were administered under strict hospital surveillance at half-hour intervals, until the cumulative daily therapeutic dose was reached.

The patient had negative skin tests except for the two controls, toluene diamine and basalm of Peru patch tests. Skin tests to the H₁-antihistamines were negative. Challenges were positive for all drugs but mizolastine and cimetidine with a pruritic maculopapular exanthema 2 (cetirizine 10 mg, loratadine 10 mg, and fexofenadine 120 mg) to 8 (mequitazine 10 mg) h after ingestion of the last dose. The symptoms rapidly disappeared after 60 mg of prednisolone.

A few skin reactions to H₁-antihistamines have been described in the literature (1–5), usually demonstrated by oral provocation tests. Some mechanisms have been suggested, including a type I IgE-mediated reaction (because of a suggestive clinical history and of positive intradermal tests to diphenhydramine and cetirizine in two cases) (2, 4), photosensitivity with phenothiazines and terfenadine (5), and paradoxical nonspecific histamine release (3). The delayed diagnosis in our patient was due to a true type IV hypersensitive reaction to hairdressing products. The allergy testing to H₁-antihistamines could not distinguish any precise mechanism, but could clearly demonstrate their responsibility and could find a well-tolerated drug of the same class.

*Maladies Respiratoires
INSERM U454
Hôpital Arnaud de Villeneuve
CHU de Montpellier
34295 Montpellier Cedex 5
France
Tel. (33) 4 67 33 61 27
Fax: (33) 4 67 04 27 08
E-mail: demoly@montp.inserm.fr

References

1. EPSTEIN E. Dermatitis due to antihistaminic agents. *J Invest Dermatol* 1949;**12**:151.
2. CARAFFINI S, LAPOMARDA V, ASSALVE D, STINGENI L, LISI P. Maculopapular eruption from cetirizine in an asthmatic patient. *Ann Ital Dermatol Clin Sper* 1996;**50**:75–76.
3. STRICKER BH, VAN DIJKE CP, ISAACS AJ, LINDQUIST M. Skin reactions to terfenadine. *BMJ* 1986;**296**:536.
4. BARRANCO P, LOPEZ-SERRANO MC, MORENO-ANCILLO A. Anaphylactic reaction due to diphenhydramine. *Allergy* 1998;**53**:814.
5. FENTON D, SIGNY M. Photosensitivity associated with terfenadine. *BMJ* 1986;**293**:823.

Histamine and LTC₄ in stinging nettle-induced urticaria

K. Taskila, J. V. Saarinen, I. T. Harvima, R. J. Harvima*

Key words: histamine; LTC₄; mediator; microdialysis; stinging nettle; wheal.

• THE symptoms caused by the stinging nettle (*Urtica dioica*), including wheal, flare, and stinging sensation, resolve slowly within hours, and are attributed to histamine derived from the plant. Serotonin and acetylcholine have also been detected in stinging nettle fluid (1). We monitored two potent wheal-forming mediators of mast cells, histamine and LTC₄, in stinging nettle-induced urticaria by the CMA-microdialysis method (2–4).

No release of LTC₄ and only weak release of histamine in stinging nettle-induced urticaria.

The skin was challenged by repeated stroking with the stem and leaves of the fresh nettle plant for about 30 s on a skin

area of 2×2 cm above the microdialysis probes that were inserted intradermally about 5 cm apart in the anterolateral aspect of the brachium. The wheal sizes were measured at 15 min by the cutting-weighing method. The wheal sizes ranged from 428 to 646 mm² (mean 529 ± 79 mm²) for the histamine probe, and from 374 to 735 mm² (530 ± 135 mm²) for the LTC₄ probe. The mean intrasubject variation was 11.9%. There was no correlation between the wheal size and detected histamine.

The stinging nettle plant extract (10% w/v in 0.9% NaCl), which contained 3360 nM (373 ng/ml) histamine, was used for skin prick and basophil histamine release tests for three subjects, and the results were negative. Previously, the nettle-hair extract with a high histamine content did not induce histamine release from dispersed mast cells *in vitro* (1).

The histamine level due to probe insertion trauma in the first 15-min fraction was 100.3 nM (range 35–240 nM, *n*=5), and this declined rapidly in the subsequent fractions to 17.3, 11.8, 11.3, 7.8, and the baseline of 5.1 ± 2.7 nM (mean ± SD, *n*=6). An immediate peak (at 15–45 min) and a weak delayed (at 90–120 min) histamine peak after the nettle challenge were detected with a wide individual variation (Fig. 1).

The histamine in the first peak was probably liberated from the mast cells. The second low histamine increase may have been due to diffusion of histamine from

stinging nettle (1) or to a delayed mediator release from the mast cells or other cells. The concentration of histamine in this study was low compared to that in our previous studies (2). In addition, to obtain a visible flare and wheal, histamine concentrations of 150–500 and 1500–5000 nM, respectively, are needed (4).

The immediate discomfort and stinging sensation after the nettle contact suggests that sensory nerves in the skin are involved and activated. These may mediate the signal with the released neuropeptides that in turn activate mast cells to release low levels of histamine, but not LTC₄ (2, 5). No changes in the levels of LTC₄ were observed in the fractions after the insertion of the microdialysis probes (up to 90 min), nor after the stinging nettle exposure. However, under identical microdialysis conditions, we have measured LTC₄ release (3).

Acknowledgement: The skillful technical assistance of Ms Katja Dufva is acknowledged.

*Department of Dermatology
 Kuopio University Hospital
 PO Box 1777
 FIN-70211 Kuopio
 Finland

Accepted for publication 15 February 2000
 Allergy 2000; 55:680–681
 Copyright © Munksgaard 2000
 ISSN 0105-4538

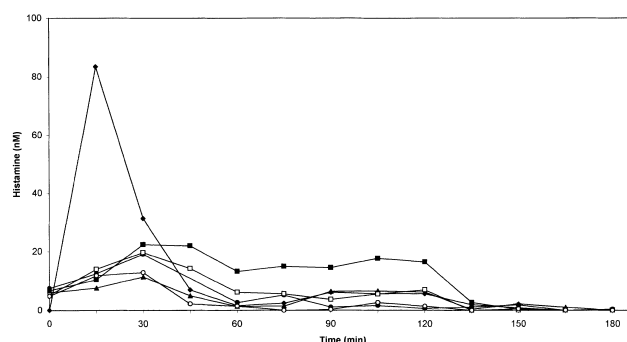


Figure 1. Histamine in 15-min microdialysis fractions after 30-s challenge with stinging nettle in six subjects (F20, F24, F26, F37, M37, and M40). Flow rate was 4.4 µl/min.