

Terfenadine in allergic chronic cough in children

We have evaluated 20 children with chronic allergic cough, refractory to conventional drugs, on daily treatment for 3 months with terfenadine according to an open design.

This pilot study was suggested by three preliminary considerations: 1) the changing role of antihistamines in the treatment of asthma, due to the new very potent compounds which are non-sedating and, in addition, some of them have been proved to exert anti-allergic properties (2, 5); 2) cough is frequently a concomitant symptom of asthma or, sometimes, it may be the unique symptom of allergic asthma either in adults and in children (1, 3); 3) histamine directly triggers the cough irritant receptors (4).

All patients (14 males and 6 females), aging from 4 to 13 years old, showed positive skin prick test and RAST to *Dermatophagoides pteronissynus*; in addition, symptoms of chronic cough dated from 1 to 36 months prior to the observation.

According to their body weight, the patients were given terfenadine suspension 1 mg/kg/bid for 3 consecutive months, after a 1-month run-in period. The severity and frequency of cough attacks were scored

daily by the patient or parents on a diary card (according to an arbitrary semiquantitative scale from 0 for no symptoms to 3 for the maximum intensity); the investigator examined the patients monthly.

Compared with the 4-week baseline observation, either severity and frequency of cough attacks were progressively reduced from the first week of treatment to the endpoint ($p < 0.01$, Wilcoxon test) (Fig. 1). No adverse effect was reported during the study.

The results of this pilot trial suggest that terfenadine may be a helpful drug for the management of refractory allergic chronic cough in children, at the dosage currently recommended for clinical use.

These preliminary data encourage further investigations in this field according to a double-blind and controlled design.

References

1. O'CONNEL EJ, ROJAS AR, SACHS MI. Cough-type asthma: a review. *Ann Allergy* 1991; 66: 278-82.
2. HOLGATE ST, FINNERTY JP. Antihistamines in asthma. *J Allergy Clin Immunol* 1989; 83: 537-47.

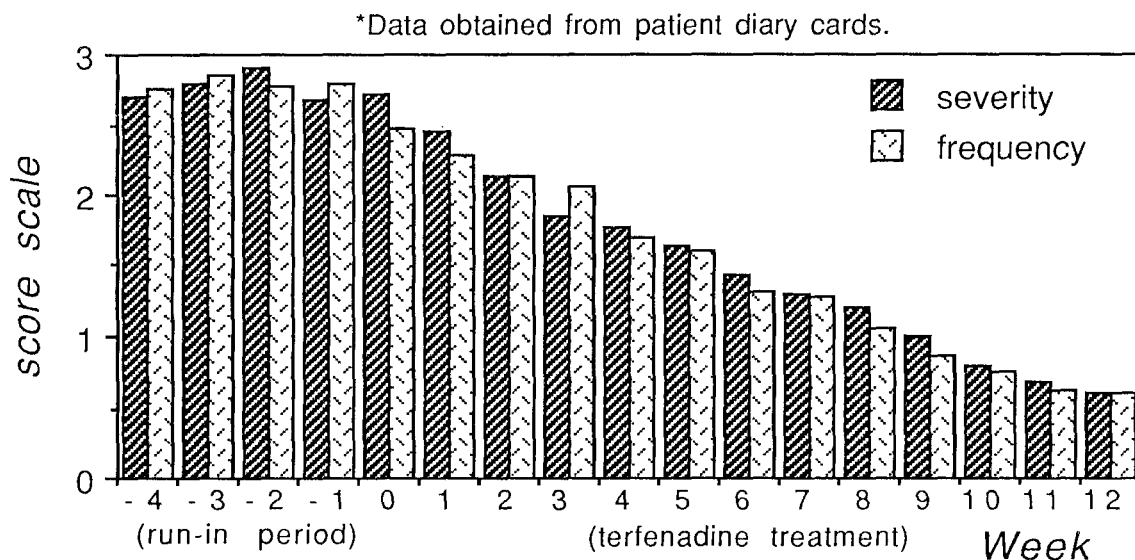


Fig. 1. Mean weekly symptom score of cough severity and frequency*.

3. YAHAV Y, KATZNELSON D, BENZARAY S. Persistent cough – a form – fruste of asthma. *Eur J Respir Dis* 1982; 63: 43–6.
4. SAMPSON SR. Sensory neurophysiology of airways. *Am Rev Respir Dis* 1977; 115: 107–15.
5. TAYTARD A, BEAUMONT D, PUJET JC, et al. Treatment of bronchial asthma with terfenadine: a randomized controlled trial. *Br J Clin Pharmacol* 1987; 24: 743–6.

G. Ciprandi, M.A. Tosca, A. Iudice, S. Buscaglia, L. Fasce, G.W. Canonica
 Allergy and Clinical Immunology Service
 Dept. of Internal Medicine, University of Genoa
 V. le Benedetto XV, 6
 Genoa 16132
 Italy

Peranaesthetic anaphylactoid shock due to mannitol

Allergic and pseudoallergic reactions due to anaesthetics, especially muscle relaxants, are well known. We investigated a case of severe anaphylactoid shock during general anaesthesia, in which mannitol appears to have been the causative agent.

A 40-year-old man had to undergo retromaxillary tumour resection. Two general anaesthetics had previously been done without any complications. There was no history of asthma or atopy. Anaesthesia was realized with thiopental, suxamethonium, fentanyl, alcuronium and an ethrane-inhalation-mixture. The induction period passed uneventfully. About 90 min after intubation, before surgical intervention, an infusion of 20% mannitol (100 ml) was given. Minutes later, hypotension and tachycardia suddenly appeared, followed by ventricular fibrillation. No cutaneous changes or bronchospasm were observed. Immediate cardiopulmonary resuscitation with catecholamines and repeated defibrillation were successfully initiated; the patient recovered the same day without any sequelae.

An allergological study was carried out 8 weeks later. Routine skin tests and RAST determinations (Phadebas, Pharmacia) with common inhalant allergens as well as with latex, thiopental and suxamethonium were negative. Prick tests with thiopental (50 mg/ml), suxamethonium (10 mg/ml), alcuronium (5 mg/ml), fentanyl (0.05 mg/ml) and mannitol (200 mg/ml equal 1.1 M) – all tested in their commercial forms – were negative. Intradermal testing at a 1:100 dilution revealed a clear positive reaction (wheal of 7 mm diameter with flare) only to mannitol. Control testing in 10 voluntary persons at the same mannitol concentration resulted in all negative. Consecutively, the *in vitro* leukocyte histamine release (HR) induced by the drugs in serial 10-fold dilutions was studied; histamine was measured by a RIA-method (5) using a commercial assay (Immunotech). Mannitol induced 20% HR of total leukocyte histamine in the 1.1 molar solution and 9% in

the 0.1 molar dilution. Controls ($n = 14$) with normal donor cells showed higher HR in 8 cases (57%) to nondilute mannitol ($18.6\% \pm 10.6$, mean $\pm$ SD), but there was practically no HR to the 0.1 molar dilution ($1.0\% \pm 1.3$). Only thiopental also induced HR: 40% in the nondilute and 7% in the 10-fold dilute solution. Here controls revealed similar results to both concentrations (32.9 ± 21.9 and $6.2\% \pm 6.5$) (Table 1).

From the clinical development, the positive specific skin test, and the higher tendency to release histamine in a 0.1 molar concentration, we concluded hypersensitivity to mannitol as the cause of this life-threatening anaphylactoid reaction. In spite of the widespread use of mannitol, only 5 cases of hypersensitivity have been reported (1–4, 6). The induced HR by hyperosmolar (1.1 M) mannitol also in normal controls demonstrates its potency to liberate histamine as previously reported by Findlay et al. (2). Thus the incident might be aggravated by the foregoing use of other histamine releasing drugs as thiopental and suxamethonium. Further studies will be necessary to elucidate the mechanism of – probably IgE-mediated – hypersensitivity in this pa-

Table 1. Percent histamine release induced by mannitol and thiopental

	Patient	Controls	
		Atopic ($n=7$)	Nonatopic ($n=7$)
Mannitol:			
20 mg/ml	9	0.6 ± 0.8	1.4 ± 1.6
200 mg/ml	20	17.7 ± 9.9	19.6 ± 12.1
Thiopental			
5 mg/ml	7	6.6 ± 6.3	5.9 ± 7.2
50 mg/ml	40	39.0 ± 26.5	26.7 ± 15.9

All values are given after deduction of spontaneous histamine release (mean $\pm$ SD).
 Atopic: mean age 32.6 years (21–55y); nonatopic: mean age 32.6 y (19–51y).

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.