

Short Communication

Contact allergy to antihistamines is not common

A. GOOSSENS AND G. LINSEN

Department of Dermatology, Leuven University Hospital, Katholieke Universiteit Leuven, B-3000 Leuven, Belgium

Key words: topical antihistamines; allergic contact dermatitis; cross-reactions; medicaments. © Munksgaard, 1998.

Topical antihistamines are available as creams, lotions, eyedrops, nasal preparations, aerosols, and suppositories. Antihistamines (or H₁-receptor antagonists) have antipruritic properties, a mild local anesthetic effect and may also diminish capillary permeability. They can be classified into 6 groups by their chemical structure (1): alkylamines, ethanolamines, ethylenediamines, phenothiazines, piperazines, and other H₁-receptor antagonists. Application to the skin is generally considered to carry an unacceptably high risk of sensitization (1, 2). Recently, several cases have been reported of allergic contact dermatitis from topically-applied doxepin hydrochloride, a tricyclic antidepressant that has very potent antihistaminic activity (3–5).

Patients and Methods

Between January 1978 and December 1997, 12,460 patients were patch tested in our Contact Allergy Unit. When contact allergy to topical antihistamines was suspected, the individual ingredients, including the antihistamines as raw materials from the manufacturers, were tested whenever possible. In view of its frequent use in Belgium, promethazine was added to the Belgian standard series from January 1978 until May 1981, and tested in 1823 subjects. 2 subjects with a positive reaction to diphenhydramine were further tested with its chemical derivatives to check for cross-sensitivity. Chlorpromazine was also tested in some subjects suspected of promethazine sensitivity.

Results

The antihistamines to which positive reactions were observed during this 20-year period are given in Table 1. Many weak phototoxic and irrelevant reactions to promethazine and chlorpromazine observed are omitted. Of the 14 patients who reacted to promethazine, 12 had an allergic contact reaction, one a photoallergic reaction, and one photoaggravation of the positive patch test. Among the 1823 subjects routinely tested between January 1978 and May 1981, 8 (0.4%) reactions to promethazine were noted (including 1 photoallergic reaction). 3 pa-

tients tested with chlorpromazine reacted positively to promethazine as well. In the 2 patients allergic to diphenhydramine and tested with chemically-related derivatives, 2 positive reactions were observed to bromodiphenhydramine, 2 to medrylamine (4-methoxydiphenhydramine) and 1 to dimenhydrinate (diphenhydramine teoclate) and p-methyldiphenhydramine, respectively.

Discussion

Allergic contact reactions in patients to antihistamine preparations have been reported, mainly to antazoline, mepyramine and tripeleminamine (ethylenediamines), diphenhydramine (ethanolamines), promethazine (phenothiazines), and phenindamine (unclassified H₁-receptor antagonists). Such reactions may also be occupational (6). We found that promethazine caused most of our reactions, followed by diphenhydramine, and clemizole, the last of which being used in topical antihemorrhoidals. We were able to demonstrate cross-reactions between diphenhydramine and some of its derivatives, as well as between promethazine and chlorpromazine. 2 patients with photocontact allergy, one to promethazine, the other to mequitazin, reacted to systemic preparations containing them.

Allergic contact and photoallergic reactions to topical antihistamines are rare, relative to their use. Phototoxic

Table 1. Positive patch tests to antihistamines (1978–1997)

promethazine ^{a)}	14 (including 2 photoallergic reactions)
diphenhydramine	8
clemizole	6
bromodiphenhydramine ^{b)}	2
medrylamine ^{b)}	2
p-methyldiphenhydramine ^{b)}	1
dimenhydrinate ^{b)}	1
dimethindene	1
mequitazine ^{c)}	1 (photoallergic reaction)

^{a)} Phototoxic reactions to promethazine (as well as to chlorpromazine) are not included.

^{b)} The primary sensitizer in both cases was diphenhydramine.

^{c)} A phenothiazine derivative used only systemically.

reactions seem to be more common and are mainly due to promethazine.

References

1. Martindale. *The Extra Pharmacopoeia*. London, The Pharmaceutical Press, 30th edition, 1993: 926–947.
2. De Groot A C, Weyland J W, Nater J P. *Unwanted effects of cosmetics and drugs used in dermatology*. Amsterdam: Elsevier, 1994: 83–85.
3. Aguirre A, Vicente J M, Zabala R et al. Eccema alérgico de contacto por doxepina tópica. *Boletín informativo del GEIDC* 1996; 24: 33–34.
4. Greenberg J H. Allergic contact dermatitis from topical doxepin. *Contact Dermatitis* 1995; 33: 281.
5. Shelly W B, Shelly E D, Talanin N Y. Self-potentiating allergic contact dermatitis caused by doxepin hydrochloride cream. *J Am Acad Dermatol* 1996; 34: 143–144.
6. Szolar-Platzer C, Maibach H. Allergic contact dermatitis to topically applied antihistamines. *Dermatosen* 1996; 44: 205–212.