

Short Communication

Severe allergic contact blepharoconjunctivitis from phenylephrine in eyedrops, with corresponding T-cell hyper-responsiveness in vitro

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Causes of allergic contact reactions of the eye region include topical medicaments, contact lens solutions, eye cosmetics and contaminated towels, pillows or fingers (1–3). Lesions may also arise from airborne or systemic contact, as well as photocontact dermatitis (4, 5). Ophthalmic drugs contain a wide range of potential allergens (6, 7).

Patient and Methods

A 76-year-old man presented with 2 episodes of blepharoconjunctivitis and periocular dermatitis 2 weeks apart. In each case, symptoms had arisen within a few hours of ophthalmological examination and had gradually resolved over the next few days on topical corticosteroid therapy. Some days before the 1st episode, a lipid-lowering agent containing simvastatin had been prescribed, but its discontinuation was followed by the 2nd episode. There was no personal or family history of atopy or previous hypersensitivity reactions.

Prick tests were performed on the flexor forearms with a standard series of aeroallergens, natural latex milk, and the eyedrops used: Neosynephrin-POS[®], Mydratikum Stulln[®], Conjuncain EDO sine[®], and Fluorescein 20%[®]. All ophthalmic preparations were tested undiluted. Reactions were read after 20 min and 2 days.

Patch testing was carried out according to the guidelines of the German Contact Allergy Group on the upper back with the following preparations: standard series, vehicles, fragrances, disinfectants, preservatives, ophthalmics, eye cosmetics, and the patient's eyedrops (undiluted; after skin stripping).

For the lymphocyte proliferation assay, peripheral blood mononuclear cells (PBMC) of the patient and of 4 healthy controls were isolated by density centrifugation (Ficoll Paque[®] Pharmacia, Sweden) and resuspended at 10^6 cells/ml in enriched RPMI 1640 culture medium containing 10% fetal calf serum (Sigma, Germany). Stimulation assays were performed in microtiter plates (Nunc, Denmark) in triplicate (each using 2×10^5 cells/well) with medium alone or in the presence of phytohemagglutinin (PHA, 2 μ g/ml), tetanus toxoid (TT, 5 μ g/ml) or phenylephrine hydrochloride (1 μ g/ml). After 3 days of culture, tritiated thymidine was added. Incorporated radioac-

tivity was determined 16 h later by scintillation counting and expressed in relation to medium control cultures as a stimulation index (SI).

Results

Prick testing showed a reaction at 20 min only to the histamine control. Patch testing gave reactions to fragrance mix (8% pet.; D2: – D3: +), povidone-iodine (10% aq.; D2: – D3: +), phenylephrine hydrochloride (10% aq.; D2: +, D3: ++; no reaction in 10 controls) and Neosynephrine[®] eyedrops containing 5% phenylephrine (D2: +; D3: ++). Concomitantly (at the D2 reading), an eczematous reaction was observed at the prick test site with the phenylephrine-containing eyedrops. 1 day later, dermatitis had spread over the proximal half of the patient's forearm. At the same time, a flare-up dermatitis, involving the forehead and periocular regions, developed. The proliferative responses in vitro of PBMC of the patient and the controls to the vari-

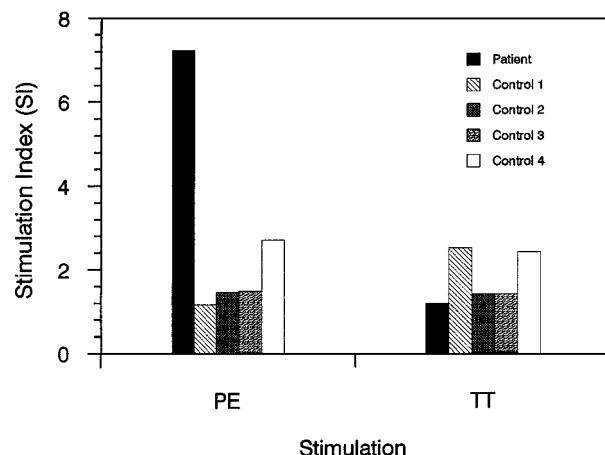


Fig. 1. Proliferative response expressed as stimulation index (SI) of peripheral blood leukocytes from the patient and 4 controls to phenylephrine (PE, 1 μ g/ml) or tetanus toxoid (TT, 1 μ g/ml). Mean SI to phytohemagglutinin (PHA) was 30.6 (range: 14.1–61.2).

ous stimuli are shown in Fig. 1. The patient's cells showed enhanced specific proliferation on stimulation with phenylephrine hydrochloride (SI=7.2), in contrast to those from the healthy controls (SI 1.2 to 2.8). The similarly low proliferation in vitro of both the patient's and the control's PBMC to TT reflects diminishing immunization status (for all individuals, last booster immunization >10 years ago) in contrast to PHA-induced proliferation. The mean SI of the response to PHA for all individuals tested was 30.6 (range: 14.1–61.2).

Discussion

Allergic contact dermatitis due to the sympathomimetic compound phenylephrine is a rarely reported complication of its use in ophthalmic preparations (8–10) and may occasionally also be encountered on application in other locations (11–13).

Flare-up reactions at sites of previous lesions (apart from external allergen contact) can be seen in systemic contact dermatitis or fixed drug eruption or may rarely be encountered as recall dermatitis after immunomodulatory manoeuvres such as radiotherapy or chemotherapy (14, 15). The enhanced proliferative response in vitro of the patient's PBMC to phenylephrine is in accordance with similar findings reported by Geyer et al. (16). Thus, phenylephrine has to be considered a potentially strong contact allergen.

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References

1. Dohn W, Brinkmann J. Contact dermatitis in the eye region. *Akt Dermatol* 1989; 15: 284–287.
2. Herbst R A, Malbach H I. Contact dermatitis caused by allergy to ophthalmic drugs and contact lens solutions. *Contact Dermatitis* 1991; 25: 305–312.
3. Doods-Gossens A. Cosmetics as causes of allergic contact dermatitis. *Cutis* 1993; 52: 316–320.
4. Doods-Gossens A. The red face: contact and photocontact dermatitis. *Clin Dermatol* 1993; 11: 289–295.
5. Gonçalo M, Ruas E, Figueiredo A, Gonçalo S. Contact and photocontact sensitivity to sunscreens. *Contact Dermatitis* 1995; 33: 278–280.
6. Herbst R A, Malbach H I. Contact allergy caused by allergy to ophthalmics: an update. *Contact dermatitis* 1992; 27: 335–336.
7. Tabar A I, Garcia B E, Rodriguez A, Quirce S, Olaguibel J M. Etiologic agents in allergic contact dermatitis caused by eyedrops. *Contact Dermatitis* 1993; 28: 50–51.
8. Barber K A. Allergic contact eczema to phenylephrine. *Contact Dermatitis* 1983; 9: 274–277.
9. Ducombs G, De Casamayor J, Verin P, Maleville J. Allergic contact dermatitis due to phenylephrine. *Contact Dermatitis* 1986; 15: 107–108.
10. Antbarro B, Barranco P, Ojeda J A. Allergic contact blepharoconjunctivitis caused by phenylephrine eyedrops. *Contact Dermatitis* 1991; 25: 323–324.
11. Thomas P, Rueff F, Przybilla B. Allergic contact dermatitis from phenylephrine in a phlebological ointment. *Contact Dermatitis* 1995; 32: 249–250.
12. Bardazzi F, Tardi M, Mariani R, Rapacchiale S, Valenti R. Phenylephrine in eardrops causing contact dermatitis. *Contact Dermatitis* 1991; 24: 56.
13. Wilkinson S M, Kingston T P, Beck M H. Allergic contact dermatitis from phenylephrine in a rectal ointment. *Contact Dermatitis* 1993; 29: 100–101.
14. El Sayed F, Bazex J. Airborne contact dermatitis from chromate in cement with recall dermatitis on patch testing. *Contact Dermatitis* 1994; 30: 58.
15. Anderson L L, Welch M L, Grabski W J. Allergic contact dermatitis and reactivation phenomenon from iontophoresis of 5-fluorouracil. *J Am Acad Dermatol* 1997; 36: 478–479.
16. Geyer O, Neudorfer M, Lazar M, Dayan M, Mozes E. Cellular sensitivity in allergic blepharoconjunctivitis due to phenylephrine eye drops. *Graefes Arch Clin Exp Ophthalmol* 1993; 231: 748–750.