Doubtful Value of Patch Testing for Suspected Contact Allergy to Ophthalmic Products

Monica Corazza[1], Lucetta Taddei Masieri[2] and Annarosa Virgili[1]
[1]*Department of Clinical and Experimental Medicine, Section of Dermatology, and* [2]*Department of Ophthalmology, Azienda Hospital, University of Ferrara, Via Savonarola 9, IT-44100 Ferrara, Italy. E-mail: Czm@unife.it*
Accepted August 9, 2004.

Sir,

Allergic contact dermatitis is the most common cause of peri-orbital eczema (1). It may be caused by allergens brought in contact with the eyelids by hand transfer (like toluene sulfonamide-formaldehyde resin in nail polishes), by airborne contact (like sesquiterpene lactones) or, most frequently, by direct application of cosmetics or topical ophthalmic medicaments. The percentage of sensitization due to cosmetics, such as moisturizing creams or eye-shadows, is estimated to range from 2.5% to 26% (2, 3). However, topical ophthalmic drugs, eye drops and contact lens solutions play a considerable role too. We studied 62 patients with eyelid dermatitis, closely related to the use of topical ocular products, with the aim of discerning the role of ophthalmic products in eyelid allergic contact dermatitis.

PATIENTS AND METHODS

Over a 65-month period 62 patients were affected by peri-orbital dermatitis while using topical ocular products (eye drops, ophthalmic ointments, contact lens solutions). The patients (21 men and 41 women), mean age 58.3 years (range 21–86), had eczema localized to the eyelids (39 patients), persistent erythematous-oedematous reaction of the eyelids (21 patients), or conjunctivitis (2 patients) after the use of such products.

The correlation between specific involvement of the eye or the skin surrounding the eye and local application of ophthalmic drugs or contact lens solutions was suggested by a clinically relevant history of intolerance to ophthalmic products, or by a positive stop-restart test.

Ophthalmologic therapies had been prescribed for glaucoma (39 cases), conjunctivitis (13 cases), Sjögren syndrome (3 cases), intolerance to contact lenses (4 cases), cataract (1 case) and infection of lacrimal ducts (2 cases).

Atopy was found in 11 patients, but only one patient had clearly atopic allergic rhinoconjunctivitis. However, this patient experienced worsening of eyelid dermatitis after using topical ophthalmic products. Fifty-seven patients used eye drops and/or ointments, the others used tear drops or contact lens solutions.

The allergological investigation was carried out by patch tests with the standard Italian Società Italiana di Dermatologia Allergologica Professionale ed Ambientale (SIDAPA) (www.sidapa.com) series and with the preservatives series. We also performed patch tests with a series of topical ophthalmic products: sodium EDTA 1% pet., monobasic sodium phosphate 1% aq., hydroxypropylcellulose 25% alc., hydroxyethylcellulose 25% alc. and dibasic sodium phosphate 1% aq. We prepared this series using the most common constituents present in eye drops. Patch tests were also carried out with the commercial ophthalmic medicaments and eye drops used by the patients and tested as is. Patch tests were applied in Finn Chambers® (Epitest, Oy, Tuusula, Finland) on Scanpor® tape (Alpharma AS, Oslo, Norway) for 48 h and were read on days 2 and 3; clinical scoring was according to International Contact Dermatitis Research Group recommendations (1). Each positive reaction was evaluated as a possible causative role for the eyelid dermatitis (time association, known exposure, presence of the allergen in products previously used) and judged relevant or not.

RESULTS

A total of 43 positive reactions were found to standardized allergens (36 in the SIDAPA standard series and 7 in the preservatives series) in 25 patients.

In the SIDAPA series, 9 patients had an allergic reaction to thimerosal, but thimerosal was relevant in only 6 cases as it was a component of the ophthalmic products previously used by the patients. Three other positive relevant reactions were detected to allergens contained in cosmetics: formaldehyde, methylisothiazolinone/methylchloroisothiazolinone (Kathon CG) and cocamidopropyl betaine.

In the preservatives series, we found 7 positive, but non-relevant reactions. Patch tests performed with the constituent series were negative in all the 62 patients.

A total of 210 patch tests in 50 patients were carried out with the patients' own ophthalmic products. Only 15 positive reactions were detected in 12 subjects, 2 showing multiple sensitizations. Fourteen reactions were found to commercial eye drops containing, respectively, befunolol (three), timolol (two), betaxolol (one), latanoprost (two), tropicamide and phenylephrine (two), apraclonidine chlorhydrate (one), levocabastine chlorhydrate (one), tetrizoline and pheniramine (one), dorzolamide (one). One reaction was found on testing a contact lens solution containing thimerosal. All these positive reactions to the patients' own products were considered relevant for the dermatitis.

DISCUSSION

In the literature numerous reports confirm the relevant role of allergic contact dermatitis in eyelid eczema with sensitization ranging from 24% to 72% (4–10). The differences largely depend on the selection of patients and the number of allergens applied. In all studies the selection of patients was based on clinical manifestations of eczema on the eyelids. Metals like nickel sulphate, cosmetic ingredients (fragrances, Kathon CG, toluene

sulphonamide formaldehyde resin), antibiotics and preservatives in topical ophthalmic products (thiomerosal, gentamycin and neomycin) were the most common allergens (5–8).

In the present study we only included patients with a strong suspicion of allergy to topical ophthalmic products. All the patients were submitted to a large battery of allergens. Herbst & Maibach (11) have reviewed the literature and proposed an 'ophthalmic series' with both active drugs and antimicrobial preservatives, known as possible causative agents of allergic contact reactions. We included all the preservatives and antimicrobials present in Herbst's tray (11).

Even though we considered them to be weak allergens we also performed tests with our 'constitutive series'. To our knowledge these substances had never been systematically tested before.

Having prepared this detailed battery of allergens and performed patch tests in only very selected patients, a wide number of positive reactions was expected. We observed 43 positive reactions, but the number of relevant positive reactions was scarce. Some allergens reflected an environmental exposure or cosmetic use and were not related to the use of ophthalmic medicaments. No reactions were detected to antibiotics like neomycin.

As already reported by others (7) thiomerosal was the most frequent relevant preservative observed. The percentage of sensitization to thiomerosal in patients affected by periorbital eczema is 6.6% (7). Although some authors have reported a prominent incidence of thiomerosal allergy in women (12), this was not observed in our study.

Surprisingly, benzalkonium chloride and phenylmercuric salts allergens commonly found in ophthalmic preparations always gave negative reactions.

Testing with the patients' own ophthalmic products proved to be quite a time-consuming practice. Of our patients, 19% were positive to their own preparations, a result similar to the 23% reported by others (7). Although some reports emphasize the failure of testing with eye drops containing beta-blocking agents (13, 14), in our study the highest number of positive reactions was found to eye drops containing these molecules (six reactions).

In accordance with our previous observations in a smaller series of patients (15), we underline the fact that negative patch tests results are common despite the history given by the patients.

Irritative reactions due to topical ophthalmic products, especially beta-blocking agents and contact lens solutions, cannot be ruled out. In fact, previous reports evidenced irritative dermatitis in 21% of patients with peri-orbital dermatitis (7).

Even though the results are often negative, patch tests remain the first step in diagnosing a suspected allergy to ophthalmic compounds. Admittedly, the very low concentration of allergens in commercial products could be insufficient to elicit an allergic reaction on the back, and the anatomical and physiological properties of eyelid skin, sometimes previously damaged by dermatitis, may cause a lower threshold to allergy in comparison with the thick healthy skin of the back. Therefore, scratching or stripping the skin of the back could be a second step after conventional patch tests (11). These new procedures of testing should be carried out in patients who suffer from chronic pathologies, like glaucoma, who often need prolonged therapies with ophthalmic medicaments.

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