

Allergic contact dermatitis and conjunctivitis from epinephrine

SAFWAT D. ALANI¹ AND MILIJM D. ALANI²

¹ Department of Ophthalmology, Sahlgren's Hospital, University of Gothenburg, Gothenburg, Sweden

² Department of Dermatology, Baghdad University, Baghdad, Iraq

A patient with chronic open-angle glaucoma was suspected of having allergic dermatitis and conjunctivitis to epinephrine. He was tested with epinephrine and other active substances, the preservatives and antioxidants usually used in the preparation of eye drops. He was also tested with other possible contactants with which he had had contact.

The patient showed positive allergic patch test reactions to the chloride solution of epinephrine. The patient showed an unexpected positive reaction when tested with di-isopropyl fluorophosphate (DFP).

The importance of routine patch testing in ophthalmic practice to detect sensitizers in cases of contact allergy is stressed.

Key words: allergic conjunctivitis – contact dermatitis – DFP sensitivity – epinephrine sensitivity – patch testing.

Received for publication December 8, 1975

For more than sixty years epinephrine has been used as eye drops to lower the intra-ocular pressure in cases of open-angle glaucoma. However, during the last fifteen years reports have been published describing the undesirable reactions it causes such as a burning sensation, orbital pain, conjunctival injection and epiphora.

Ophthalmologists are familiar with the side effects of epinephrine. Their familiarity is solely based on clinical observations (Becker & Ley 1958, Byron 1960, Becker et al. 1961, Vaughan et al. 1961, Ballantine & Garner 1961, Becker & Morton 1966). Allergic reactions have been mentioned but skin tests have been performed in only two cases reported (Colldahl & Fagerberg 1956, Gibbs 1970). Circulating anti-epinephrine

antibodies were demonstrated (Aronson & Jamamoto 1966).

This report describes a case of sensitivity to epinephrine eye drops and the skin patch tests which were performed to confirm the clinical observation.

Case Report

A 74-year-old man, without any history of allergic disease, had been treated for simple open-angle glaucoma with epinephrine bitartrate since July 1966. Two years later, in August 1968, contact dermatitis was noted on the eyelids. The dermatitis promptly receded when epinephrine drops were stopped. Pilocarpine and later a pilocarpine-physostigmine mixture were pre-

scribed. In May 1969, the patient complained of ocular discomfort and conjunctival injection and was treated with topical hydrocortisone cream. The symptoms were ascribed to irritative conjunctivitis caused by pilocarpine or physostigmine. The patient was therefore treated with epinephrine borate drops instead. In September 1970, the patient was admitted to the department because of severe exacerbation of persistent contact dermatitis and conjunctivitis, in spite of treatment with different topical corticosteroids, i.e. hydrocortisone acetate, prednisolone and fluocinolone acetonide.

The patient complained of itching, burning

sensation, foreign body sensation and tearing. On examination he showed red confluent papules with fine scales on the eyelids, lower part of the forehead, root of the nose and upper part of the cheeks. The lids were swollen with reddened margins. The bulbar conjunctiva was injected with slight chemosis, and the conjunctival blood vessels were engorged. The lower palpebral conjunctiva showed diffuse injection. No follicular conjunctival reaction could be detected.

The eyedrops were discontinued and the patient was relieved of his symptoms; the dermatitis receded within the next few days.

Table 1. Ophthalmic routine patch test series for patients with glaucoma

Test substance	Concentration %	Concentration %	Results of patch tests
<i>Active substances:</i>			
Epinephrine chloride	1.0	0.1	+++
Pilocarpine chloride	1.0	0.1	—
Physostigmine salicylate	1.0	0.5	—
Synstigmine bromide	1.0	0.1	—
Carbacholine chloride	1.0	0.1	—
Tosmilen bromide	2.5	0.5	—
Mintacol	1.0	0.1	—
Echothiophate	1.0	0.1	—
DFP	0.25/peanut oil	0.1/peanut oil	+++
Acetazolamide	1.0 /petrolatum	0.1/petrolatum	—
Dichlorphenamide	1.0 /petrolatum	0.1/petrolatum	—
<i>Antioxidants, bacteriostatics and vehicles:</i>			
Benzalkonium chloride	0.1	0.01	—
Boric acid	5.0/glycerin	3.0	—
Chlorobutanol anhydrous	2.0/alcohol	1.0/alcohol	—
Cetylpyridinium chloride	0.1	0.01	—
Methyl-para-oxybenzoate	5.0/alcohol	0.5/alcohol	—
Propyl-para-oxybenzoate	5.0/alcohol	0.5/alcohol	—
Sodium pyrosulphite	1.0	0.1	—
8-hydroxyquinoline sulphate	5.0/petrolatum	2.0/petrolatum	—
Phenylmercuric nitrate	0.1/petrolatum	0.01	—
Phenylmercuric acetate	0.1/petrolatum	0.01	—
Di sodium edetate	5.0	1.0	—
Mannitol	5.0	2.0	—
Hydroxypropylmethyl-cellulose	as is	—	—
Arachis oil (peanut)	as is	—	—
Adeps lanae	as is	—	—

All substances are in aqueous solutions unless otherwise stated.

Table 2. Complement patch test series

Test substance	Concentration	Results of patch tests
<i>Rubber additives</i>		
Tetramethylthiuramdisulphide (TMTD)	2 % in petrolatum	—
Tetramethylthiurammonosulphide (TMTM)	2 % in petrolatum	—
Mercaptobenzothiazole (MBT)	2 % in petrolatum	—
<i>Substances from the container of epinephrine borate drops</i>		
Rubber of the dropper bulb	powder, as is	—
Plastic of the cap	powder, as is	—
<i>Generic names</i>		
Demecarium bromide:	Tosmilen	
Di-isopropyl fluorophosphate:	DFP	
Diethyl-p-nitrophenyl phosphate:	Mintacol	

The patient was patch-tested with different substances to detect the offending sensitizer.

Method

Routine patch testing was carried out on patients with ocular allergic manifestations (Alani 1971).

Table 1 shows the routine ophthalmic patch test series used for patients with glaucoma. The series includes active substances, antioxidants, bacteriostatics and vehicles of eye drops usually prescribed for patients with glaucoma.

In this case the patient was patch-tested with:

1. Routine ophthalmic series (Table 1).
2. Rubber additives and powdered rubber from the dropper bulb of the epinephrine drops (Table 2).
3. The plastic from the cap of the epinephrine eye drops bottle, applied as powder (Table 2).

Results

The patch testing showed a positive allergic reaction to epinephrine chloride. The antioxidants and bacteriostatics found in the

epinephrine drops used by the patient, i.e. boric acid, phenylmercuric acetate, sodium pyrosulphite and 8-hydroxyquinoline sulphate gave negative results (Table 1).

The positive patch test reaction to epinephrine persisted for about nine days after removal of the patch.

On discontinuing epinephrine borate drops, however, the patient was relieved of his symptoms within the next two days. The dermatitis and conjunctivitis receded in the course of the next few days.

The patient was found to have an unexpected allergic positive test reaction when tested with DFP in peanut oil. The positive reaction to DFP was erythema and infiltration with minute papules. The skin test erythema persisted for about fourteen days after removal of the patch. No history of contact with pesticides of the organophosphate group was reported which could explain this sensitivity to DFP as of the cross-sensitivity type.

Discussion

Many ophthalmic drugs are potent contact sensitizers. In practice, ophthalmologists do not use patch testing as a diagnostic tool to

determine the causative allergens in such suspected cases of sensitivity. The step which they usually take is to change the eye drops, relying mostly on clinical observations. This would be troublesome to patients with glaucoma whose ocular pressure was adequately controlled with the previous drops. Therefore, patients who develop orbital eczema during the course of treatment with eye drops or ointments should be patch-tested with a standard series including the common allergens usually causing dermatitis of the orbital region. The patient should also be tested with the medicaments which they use but which are not included in the series.

Many ophthalmic drugs may cause contact dermatitis or conjunctivitis. Even topical corticosteroids may prove to be sensitizers (Alani & Alani 1972, Fisher 1973, Alani & Alani 1976). Spectacle frames made of celluloid, plastic, or metal such as nickel or chrome may cause contact dermatitis of the orbital region. Therefore, patch testing in ophthalmic practice is helpful in detecting such allergens.

In the present case epinephrine proved to be the causative allergen. The patch testing supported the clinical suspicion.

References

- Alani, M. D. & Alani, S. D. (1972) Allergic contact dermatitis to corticosteroids. *Annals of Allergy* 30, 181-185.
- Alani, S. D. (1972) Diagnosis of periorbital eczematous dermatitis and allergic conjunctivitis by patch testing. *Acta Ophthalmologica (Copenhagen)* 50, 628-629.
- Alani, S. D. & Alani, M. D. (1976) Allergic contact dermatitis and conjunctivitis to corticosteroids. *Contact Dermatitis* 2, in press.
- Aronson, S. B. & Jamamoto, E. A. (1966) Ocular hypersensitivity to epinephrine. *Investigative Ophthalmology* 5, 75-80.
- Ballentine, E. J. & Garner, L. L. (1961) Improvement of the coefficient of outflow in glaucomatous eyes. *Archives of Ophthalmology* 66, 314-317.
- Becker, B. & Ley, A. P. (1958) Epinephrine and acetazolamide. *American Journal of Ophthalmology* 45, 639-643.
- Becker, B., Petit, T. H. & Gay, A. J. (1961) Topical epinephrine therapy of open-angle glaucoma. *Archives of Ophthalmology* 66, 219-225.
- Becker, B. & Morton, W. R. (1966) Topical epinephrine in glaucoma suspects. *American Journal of Ophthalmology* 62, 272-277.
- Byron, H. M. (1960) Conjunctival reaction due to L-epinephrine bitartrate (Epitrate). *Archives of Ophthalmology* 63, 567-570.
- Colldahl, H. & Fagerberg, E. (1956) Conjunctivitis and eyelid eczema due to hypersensitivity to adrenalin solution employed in spray-treatment of asthma. *Acta Allergologica* 10, 77-81.
- Fisher, A. A. (1973) *Contact Dermatitis*, 2nd ed., pp. 59-60. Philadelphia: Lea & Febiger.
- Gibbs, R. C. (1970) Allergic contact dermatitis to epinephrine. *Archives of Dermatology* 101, 92-94.

Address:

S. D. Alani, M.D.
Läkarhuset
Södra vägen 27
S-411 35 Gothenburg
Sweden

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.