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Topical β -blockers are modern anti-glaucoma drug treatment. They lower intraocular pressure by decreasing secretion of aqueous humour and increasing its outflow. Allergic contact dermatitis from topical β -blocking agents is increasing in glaucoma patients (1, 2). Identifying the contact allergen in such cases is not easy, and in the past few years, because of cross-sensitivity among the different β -blockers, it is also difficult to identify an alternative drug (3, 4).

Case report

A 45-year-old non-atopic woman, affected by a 6-year primary, open-angle glaucoma, treated in past years with levobunolol eyedrops (Vistagan[®]), presented itching dermatitis of the eyelids and periorbital areas. On examination, bilateral erythematous-squamous swelling plaques on the upper and lower eyelids were observed. These lesions persisted for 2 months in spite of topical corticosteroid treatment. Patch testing with the standard series (Società Italiana di Dermatologia Allergologica Professionale e Ambientale), eyelids series, preservative series, and the constituents of Vistagan[®] were performed, and positive reactions to levobunolol 1% aq at D2 (++) , D3 (++) , and D6 (+++) resulted. Levobunolol was discontinued and clinical manifestations completely resolved within 4 weeks. Afterwards, the patient used an ophthalmic solution containing befunolol, which had never been used previously, and developed similar lesions 7 days later. Patch testing with a series of 6 different β -blockers showed positive reaction to befunolol (Table 1).

A repeated open application test (ROAT) performed with Carteol[®] eyedrops (containing carteolol, which was negative on a patch test) on the volar aspect of the forearm for 15 consecutive days did not show positive reactions; so carteolol was administered without side-effects for 12 months.

Comment

There are different reports about cross-sensitivity among β -blockers in the past few years (5–8). Our case suggests the possibility of cross-reaction between levobunolol and befunolol, supported by the positive patch test reaction to befunolol that had never previously been used.

The chemical structure of β -blockers is similar to their physiological agonist noradrenaline; they all have a heterocyclic aromatic group, which conditions their lipophilic and stabilizing properties, and a lateral aliphatic chain, which conditions affinity to the receptor. The aliphatic chain of β -blockers, common to the various molecules, could act as an antigenic determinant. Nevertheless, Giordano-Labadie et al. report that although all β -blockers have a similar chemical structure, it could not act as a hapten (9); they hypothesize a cross-sensitivity which develops after primary metabolism to a common aldehyde. Further studies are necessary to ascertain this possibility.

There is also the problem of false-negative patch tests with β -blockers tested at 1% or with the commercial eyedrops (4): there are so many patients with clinical aspect and anamnesis strongly suggesting an allergy to eyedrops containing β -blockers but negative to patch test. This could be explained by the anatomic aspect and thickness of eyelid skin: commercial products elicit an allergic reaction in the eyelid, but

Allergic contact dermatitis due to levobunolol with cross-sensitivity to befunolol

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Table 1. Patch testing results with 7 different β blockers

		D2	D3	D6
Levobunolol	1% aqueous	++	++	+++
Befunolol	1% aqueous	+	++	++
Betaxolol	1% aqueous	–	–	–
Carteolol	1% aqueous	–	–	–
Metipranolol	1% aqueous	–	–	–
Nebivolol	1% aqueous	–	–	–
Timolol	1% aqueous	–	–	–

the same concentration, even in an occlusive patch test, will not induce a clinically evident reaction on the back. An increase of hapten concentration (3) or a 'stripped' patch test could represent a valid method to simulate the higher susceptibility of eyelid skin.

We recommend to perform patch tests both with suspected drug and alternative β -blockers series in patients with allergic contact dermatitis from β -blocking agents. Because of the possibility of false-negative patch test with β -blockers eyedrops (3), a ROAT performed twice a day for 15 days with the commercial product containing an alternative β -blocker is recommended before use (10).

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