Contact Dermatitis

ALLERGIC CONTACT DERMATITIS CAUSED BY β-BLOCKERS • HORCAJADA-REALES ET AL.

Allergic contact dermatitis caused by timolol with cross-sensitivity to levobunolol

Celia Horcajada-Reales, Virna J. Rodríguez-Soria and Ricardo Suárez-Fernández

Department of Dermatology, Hospital Universitario Gregorio Marañón 28007, Madrid, Spain
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Glaucoma after corneal transplantation is a main cause of ocular morbidity after penetrating keratoplasty. The use of topical treatments to control intraocular pressure is the first-line treatment for this sequela (1).

Contact allergy to topical β-blockers is a well-recognized side-effect of glaucoma treatment. We report a case of allergic contact dermatitis caused by the β-blocker timolol in eyedrops. Patch test result showed cross-sensitivity/co-reactivity to levobunolol.

Case Report

A 61-year-old man, with no history of atopy or allergy, had long been treated for open-angle glaucoma after corneal transplantation with eyedrops containing the β-blocker timolol and brimonidine (Combigan®), as well as ciclosporin to avoid corneal graft rejection. He developed eyelid dermatitis, associated with conjunctival hyperaemia (Fig. 1). His condition rapidly improved after the use of Combigan® had been suspended and following therapy with topical corticosteroids.

Patch testing with the TRUE Test® series and own ophthalmic medicaments (including those containing ciclosporin) ‘as is’ gave a positive reaction only to Combigan® on day (D)2 and D4. Patch tests with vehicle ingredients gave negative results. On further patch testing with a preservatives series and an ophthalmic medicaments series containing other β-blockers (MartiTor®), additional positive reactions as shown in Table 1 were found (Figs. 2 and 3).

Correspondence: Celia Horcajada-Reales, Department of Dermatology, Hospital Gregorio Marañón, c/Doctor Esquerdo, 46, 28007 Madrid, Spain. Tel: 0034 915866680. E-mail: celiahr@hotmail.com

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Table 1. Patch test results

<table>
<thead>
<tr>
<th>Medicaments</th>
<th>D2</th>
<th>D4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combigan® (brimonidine, timolol)</td>
<td>++</td>
<td>+++ (Fig. 2)</td>
</tr>
<tr>
<td>Ganfort® (bimatoprost/timolol)</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Timofot® (timolol maleate)</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Betagan® (levobunolol HCl)</td>
<td>+</td>
<td>+ (Fig. 3)</td>
</tr>
<tr>
<td>Betoptic® (betaxolol HCl)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Elebloc® (carteolol HCl)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Xalatan® (latanoprost)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Benzalkonium chloride 0.1% aq.</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Propranolol HCl 2% aq.</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Timolol 1% aq.</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Levobunolol 1% aq.</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Betaxolol 1% aq.</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Carteolol 1% aq.</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

Medicaments ‘as is’.

Fig. 1. Local oedema, erythema and desquamation in the periocular region.
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Comment

Sensitization to topical β-blockers is a well-recognized side-effect of glaucoma treatment (2–4). Contact allergy is usually attributable to single agents or, more rarely, to multiple β-blockers (5–7). This is a case report of simultaneous patch test reactions to two β-blockers after many years of timolol exposure. According to medical records, the use of levobunolol-containing drugs can be excluded in our patient, so true cross-sensitivity to levobunolol should be considered. Giordano-Labadie et al. hypothesize that cross-sensitivity between β-blockers could develop after primary metabolism to a common aldehyde (8). In a large study of β-blockers in eyedrops, co-reactions to both β-blockers were reported (9).

As patch tests showed positive reactions to drug combinations (Combigan® containing brimonidine and timolol, and Ganfort® containing bimatoprost and timolol), sensitization to the other components (9) cannot be excluded, as the patient’s history was unclear concerning previous exposure to these agents.

In our case, a normal patch test was sufficient to demonstrate contact allergy. An increase in the hapten concentration (10), scratch-patch testing (11) or pretreatment with sodium lauryl sulfate (12) could otherwise be used to avoid false-negative results (13).

Our patient developed contact allergy after many years of timolol exposure, and patch testing appeared to show cross-reactivity to levobunolol; this has been previously reported only a few times (9, 14).

Fig. 2. Positive patch test reaction at D4 to Combigan® on the lower back.

Fig. 3. Positive patch test reaction at D4 to Betagan® on the upper back.

References

14. Koch P. Allergic contact dermatitis due to timolol and levobunolol in eyedrops, with no cross-sensitivity to other ophthalmic beta-blockers. Contact Dermatitis 1995; 33: 140–141.