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Case Report

Allergy to Timolol Contained in Eyedrops for Glaucoma

Eleonora Nucera[1,2#], Angela Rizzi[2#], Riccardo Inchingolo[3*], Arianna Aruanno[2], Marinella Viola[2]

[1]Dip. Scienze Mediche e Chirurgiche, Università Cattolica Sacro Cuore, Italy

[2]UOSD Allergologia ed Immunologia Clinica, Fondazione Policlinico Universitario A, Italy

[3]UOC Pneumologia, Fondazione Policlinico Universitario A. Gemelli IRCCS, Italy

[#]Contributed Equally to this Article

[*]**Corresponding author:** Riccardo Inchingolo, UOC Pneumologia, Fondazione Policlinico Universitario A. Gemelli IRCCS, Largo Agostino Gemelli, 8-00168 Rome, Italy

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Abstract

Background: Allergic eyelid dermatitis is a common but often misdiagnosed disease that is related to eyedrops, topical cosmetics or skin care products. With regard to eyedrops, adverse reactions can be caused by both active ingredients and excipients. Identification and elimination of causative agents is the mainstay of management.

Patient and Methods: We describe the case of a woman who had been suffering from eyelid and peripalpebral dermatitis for four months. To treat her glaucoma, for a year she used several eyedrops for one year, switched by the ophthalmologist several times. She has also been reported oculorhinitis in March for some years. The patient underwent an allergological work-up consisting in prick test for inhalant allergens and patch tests with the G.I.R.D.C.A. series, benzalkonium chloride 0.1% aq., all the involved eyedrops and additional eyedrops 'as is'.

Results: The patch test for the G.I.R.D.C.A. series and benzalkonium chloride as well as prick tests for the main inhalant allergens were negative. Only patch test performed for eyedrops containing timolol - alone or in association with other active ingredients - gave a positive response.

Conclusions: In our patient with eyelid and peripalpebral dermatitis, we have ruled out an allergy to the most common contact and inhalant allergens, while we have identified a cell-mediated hypersensitivity to timolol among the several eyedrop used by the patient.

Keywords: Allergic eyelid dermatitis; Contact dermatitis; Cell-mediated hypersensitivity; Patch test; Timolol

Introduction

Adverse reactions to ophthalmic products have been frequently observed. The most common are conjunctival manifestations and eyelid dermatitis. These reactions can be caused by both active ingredients and excipients [1,2]. The main responsible drugs are parasympathomimetics, sympathomimetics, beta-blockers, carbonic anhydrase inhibitors, prostaglandin inhibitors, antibiotics, nonsteroidal anti-inflammatory drugs, and anesthetics [1,2].

Case Description

We describe the case of a 50-year-old teacher who had been suffering from eyelid and peripalpebral dermatitis for four months. To treat her glaucoma, she used several eyedrops foe one year, including Ganfort® (bimatoprost+timolol), Azarga® (brinzolamide+timolol), Iopidine® (apraclonidine), and Qualid ofta® (brimonidine). After the appearance of dermatitis, the ophthalmologist switched eyedrops several times. For a short period she also stopped all eyedrops with an improvement of dermatitis. Subsequently, she introduced first Combigan® (brimonidine+timolol) and, then, Timolabak® (timolol) with a worsening of symptoms; therefore, these eyedrops were stopped.

Finally, Latanoprost® ratiopharm Italia (latanoprost) and Azopt® (brinzolamide) eydrops were introduced without an apparent worsening of symptoms.

She has also been reported oculorhinitis in March for some years, but she denied other cutaneous diseases or allergic symptoms. The patient initially underwent an allergological work-up consisting in prick test for inhalant allergens and patch tests with the G.I.R.D.C.A. series. After a week, using Finn Chambers (SmartPractice, Phoenix, Arizona) fixed with Micropore® (3M Health Care, Borken, Germany), we patch tested benzalkonium chloride 0.1% aq., all the aforementioned eyedrops 'as is', and additional eyedrops [Saflutan® (tafluprost) and Lumigan® (bimaprost)] 'as is'. Patch tests were applied on the back and left for two days under occlusion, and readings were performed on day (D) 2 and 3 (Figure 1A). Positive patch test reactions (+, ++, or +++) were determined according to the International Contact Dermatitis Research Group (ICDRG) criteria.

The patch test for the G.I.R.D.C.A. series and the prick tests for the main inhalant allergens were negative. Therefore, we have ruled out an allergy to the most common contact and inhalant allergens. The patch tests performed for Ganfort®, Azarga®, Combigan®, and Timolabak® eyedrops were positive, while the patch tests carried out with Qualid ofta®, Azopt®, Iopidine®, Lumigan®, Latanoprost®, Saflutan® eyedrops, and benzalkonium chloride were negative (Figure 1B) (Table 1). The patient subsequently began therapy with Saflutan® eyedrop without experiencing any problems. Therefore, considering that the four patch tested positive eyedrops contained timolol - alone or in association with other active ingredients - and that the other active ingredients of associations (bimatoprost, brimonidine, and brinzolamide) were negative when individually patch tested, we have concluded for a cell-mediated hypersensitivity to timolol.

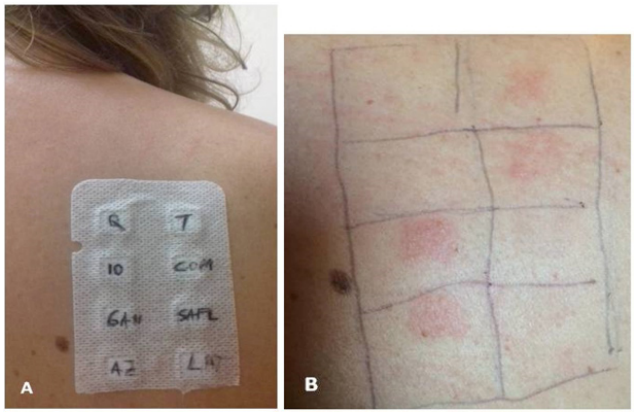

Figure 1 (A, B): The patch tests performed for Qualid ofta®, Iopidine®, Ganfort®, Azarga®, Timolabak®, Combigan®, Saflutan®, Latanoprost® eyedrops (from left, top to bottom) **(A)**. The patch test reading performed after 3days (72hours) **(B)**.

	Readings at		
	15 minutes	D2	D3
PRICK TEST:			
inhalant allergens	-		
PATCH TEST:			
G.I.R.D.C.A. series			
Combigan® 2 mg/ml+5 mg/ml (brimonidine+timolol)		-	+
Ganfort® 0.3 mg/ml+5 mg/ml (bimatoprost+timolol)		+	++
Azarga® 10 mg/ml+5 mg/ml (brinzolamide+timolol)		+/-	++
Timolabak® 5 mg/ml (timolol)		-	+
Qualid ofta® 2 mg/ml (brimonidine)		-	-
Azopt® 10 mg/ml (brinzolamide)		-	-
Ipodine® 5 mg/ml (apraclonidine)		-	-
Lumigan® 2 mg/ml (bimaprost)		-	-
Latanoprost® ratiopharm Italia 50 mcg/ml (latanoprost)		-	-
Saflutan® 2 mg/ml (tafluprost)		-	-
Benzalkonium chloride 0.1%		-	-
Eyedrops 'as is'.			

Table 1: Allergological investigation results.

Discussion and Conclusions

Allergic eyelid dermatitis is a common but often misdiagnosed disease that is related to eyedrops, topical cosmetics or skin care products. Identification and elimination of causative agents is the mainstay of management. Allergic Contact Dermatitis (ACD) caused by eyedrops is mainly attributable to active principles, but also excipients and the products "as is" should be tested. Our patient developed an ACD to timolol after almost a year. Timolol, a non-selective beta-blocker, is the most commonly used drug for the treatment of glaucoma and, for this reason, the most often involved in adverse reactions [3-5]. Patch test has proven to be a reliable method to identify an ACD caused by eyedrops and it allows to reach a diagnosis faster, especially in cases of long-lasting symptoms and ongoing multiple therapies. If conjunctivitis and/or rhinitis are also present, we suggest to perform prick test for inhalant allergens.

In conclusion, if we had overlooked the symptoms without performing an allergological evaluation, we would not have identified the responsible drug.

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Conflicts of Interest

All authors have no conflict of interest to declare.

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