

# Periocular allergic contact dermatitis caused by brinzolamide

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**KEYWORDS:** allergic contact dermatitis, brinzolamide, case report, glaucoma, periocular, Simbrinza

## CASE REPORT

A 52-year-old woman was referred to our Contact Eczema Department with right-sided, chronic, periocular eczema that had developed over the past 12 months. The patient had been diagnosed with glaucoma of the right eye 3 years earlier. Three months before developing eczema, she started Simbrinza eye drops (brinzolamide/brimonidine tartrate [Novartis Pharmaceuticals Corporation, New Jersey]). She went to the Emergency Department several times, was diagnosed with ocular herpes, and treated with oral acyclovir for 6 months without clinical improvement. Other treatments such as erythromycin (Oftalmolosa *cusí* erythromycin, Alcon, Geneva,

Switzerland) and tobramycin (Tobrex, Novartis Pharmaceuticals) also showed no satisfactory response. The patient reported intense itching and constant tearing. Microbiological cultures ruled out any infection. A repeated open application test showed positive reaction with Simbrinza eye drops at day (D) 3 (Figure 1A), while no reaction was seen with Virgan gel (ganciclovir, carbomer 974, sorbitol, benzalkonium chloride; [Thea Pharmaceuticals, Newcastle Under Lyme, UK]) until D14.

On physical examination, erythematous edema around the right eye with well-defined borders was seen (Figure 1B). An eczematous plaque on the back of the left hand was related to repeated wiping of her tearing eye (Figure 1C).



**FIGURE 1** (A) Positive repeated open application test at day 3 with Simbrinza eye drops. (B) Periocular eczematous reaction. (C) Self-transported eczematous reaction on back of the hand. (D) Positive patch test at day 4 of brinzolamide 0.1% dimethyl sulfoxide

Patch tests were performed with the European Comprehensive Baseline Series (Chemotechnique Diagnostics, Vellinge, Sweden), benzalkonium chloride 0.1% pet., propylene glycol 30% aq., carbomer 974P (Siccafluid monodose "as is"), brinzolamide 0.1% in dimethyl sulfoxide (DMSO), and brimonidine tartrate 1% DMSO. The results were interpreted according to the criteria of the International Contact Dermatitis Research Group. Patch tests were read on day (D) 2 and D4. The patient showed a positive patch test reaction to brinzolamide 0.1% DMSO (++) (Figure 1D); 10 controls tested negative.

Ocular contact dermatitis caused by brinzolamide was diagnosed. Complete improvement of the eczematous eruption was achieved within 2 weeks of discontinuing Simbrinza eye drops. The patient started latanoprost eye drops without any dermatological complication.

## DISCUSSION

Ophthalmic topical drug preparations include active ingredients and excipients. Both can cause allergic contact dermatitis,<sup>1</sup> active ingredients probably far more commonly than preservatives.<sup>2</sup>

The most common drugs reported as potent sensitizers are anti-glaucoma agents, mydriatics, antiallergics, antibiotics, antivirals, corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs), and preservatives<sup>3</sup>. Topical glaucoma medications are classified as  $\beta$ -blockers (timolol, betaxolol, carteolol, levobunolol, and brimonidine), prostaglandins (latanoprost), carbonic anhydrase inhibitors (azetazamide, dorzolamide),  $\alpha$ 2-adrenergic agonists (apraclonidine), rho kinase inhibitors (ripasudil hydrochloride hydrate), sympathomimetic (dipivefrine, apraclonidine, brimonidine), and parasympathomimetics (pilocarpine). Virtually all of these drugs have been reported to cause periocular allergic contact dermatitis (ACD).

Brinzolamide is a carbonic anhydrase inhibitor that decreases aqueous humor secretion.<sup>4</sup> This active ingredient may be found as the main ingredient (Brinzolamide Sandoz), or in combination with brimonidine (Simbrinza). Hitherto, no case related to brinzolamide has been reported.

ACD can involve the eyelids and/or conjunctiva, associated, or not, with chronic conjunctivitis or keratoconjunctivitis. Systemic manifestations may be reported by the patient.<sup>5</sup> The most common clinical sign is itchy periorbital eczema.

Patch testing is the standard method for diagnosis of periocular ACD. It is recommended to test the ophthalmic medication (active ingredient) in addition to the excipients (mainly the preservatives). Consulting the data sheet of the suspected eye drops is essential to arrive at the right diagnosis. Among the more common preservatives, benzalkonium chloride and propylene glycol can be patch tested with commercially available products. Carbomer 974P is not commercially available, but Siccafluid monodose contains this substance as the main ingredient, without containing other potentially sensitizing ingredients.

Identifying the culprit allergen and its avoidance is the basis of treatment. Topical corticosteroid treatment can be added, if necessary, although intraocular pressure should be closely monitored when treating a patient with glaucoma. Latanoprost is considered a good option in these cases, although a rare case of ocular ACD has been reported.<sup>6</sup>

We present, to the best of our knowledge, the first case of periocular ACD caused by brinzolamide. Knowing the complete composition of the eye drops is essential to performing patch tests properly.

## ACKNOWLEDGEMENTS

We acknowledge all staff working in the Contact Eczema and Immunoallergic Diseases Department, especially the specialized nurse Victor Alfredo Cassini Gómez de Cádiz.

## AUTHOR CONTRIBUTIONS

**Francisco J. Navarro Triviño:** Conceptualization; data curation; investigation; methodology; writing-original draft; writing-review and editing.

**Ricardo Ruiz Villaverde:** Supervision; writing-review and editing.

## CONFLICT OF INTEREST

The authors declare no conflict of interests.

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**How to cite this article:** Navarro-Triviño FJ, Ruiz-Villaverde R. Periocular allergic contact dermatitis caused by brinzolamide. *Contact Dermatitis*. 2020;1-2. <https://doi.org/10.1111/cod.13730>