

When ‘Preservative-Free’ Isn’t Allergen-Free: A Severe Type IV Reaction to Phenylephrine Minims

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Introduction

Type IV (delayed) hypersensitivity reactions to ophthalmic medications are rare, yet several case reports and retrospective analyses have documented that phenylephrine can trigger severe allergic contact dermatitis and blepharoconjunctivitis [1]. Preservative-free formulations have long been thought to prevent ocular toxicity and increase patient tolerability, however, young ophthalmologists can often fall into the trap of assuming that these come without risk of allergy, something we know not to be true [2].

Case Presentation

An 82-year-old female received preservative-free phenylephrine minims for routine pupil dilation. Approximately six hours later, she developed extensive periocular erythema, oedema, and dermatitis. She presented to the emergency department with marked swelling and discomfort but no visual disturbance. The clinical features were consistent with a severe delayed hypersensitivity reaction.

She was treated conservatively with cold compresses, lubricants and emollients; corticosteroids were not required. Over subsequent weeks, she experienced gradual resolution of symptoms, aligning with the expected course of a T-cell mediated type IV reaction.

The patient reported previous intolerance to several ophthalmic agents, including nepafenac and fluorescein, though she tolerated preservative-free tropicamide. This pattern supports phenylephrine itself, rather than excipients or preservatives, as the most likely trigger.

Case Images



Discussion

This case reinforces evidence that preservative-free phenylephrine is not free from allergenic potential. Severe delayed hypersensitivity reactions can result in significant periorbital inflammation and morbidity, and delayed recognition may lead to prolonged symptoms or unnecessary exposure to additional sensitizing agents. Diagnosis relies on clinical history, exclusion of alternative allergens, and patch testing when appropriate.

Although uncommon, these reports demonstrate that phenylephrine itself, independent of preservatives, can act as a sensitizer capable of inducing T-cell mediated delayed hypersensitivity. Large retrospective datasets investigating allergic contact dermatitis to ophthalmic agents further indicate that phenylephrine is among the more frequently identified sensitizers in patch-tested patients, with a notable proportion showing clinically relevant sensitisation [1].

Given the routine use of phenylephrine in ophthalmic practice, clinicians should consider it as a potential cause when patients present with periocular dermatitis following dilation, even when preservative-free preparations have been used.

Conclusion

Preservative-free phenylephrine can provoke severe type IV hypersensitivity reactions due to sensitisation to the active drug itself. Awareness, early identification, and avoidance of re-exposure are essential to prevent recurrence and chronic ocular inflammation.

[1] Svendsen, Sebastian Vigand et al. “Contact allergy to topical ophthalmic medications: A retrospective single-centre study of three decades.” *Contact dermatitis* vol. 91,2 (2024): 119-125. doi:10.1111/cod.14552

[2] Pisella, P J et al. “Prevalence of ocular symptoms and signs with preserved and preservative free glaucoma medication.” *The British journal of ophthalmology* vol. 86,4 (2002): 418-23. doi:10.1136/bjo.86.4.418