

Systemic anticholinergic side-effects

B. Wüthrich*, M. Bigler Anit, M. Kuhn,
B. Zimmerli Matter, S. Priske

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● SYSTEMIC allergic reactions to cyclopentolate, a mydriatic agent, are very rare. Munoz-Bellido et al. recently described a case of allergic contact urticaria syndrome due to cyclopentolate, and reported two other cases in the literature (1). A pharmacologic effect due to systemic absorption of this drug must also be taken in consideration.

A 34-year-old woman received 2–3 drops of Cyclogyl[®], containing 1% cyclopentolate, in each eye, as well as Novesin[®], containing 0.4% oxybuprocaine, for a routine ophthalmologic examination. Shortly after instillation, the patient experienced systemic adverse events including dizziness, weakness, tachycardia, ataxia, nausea, asthenia, agitation, and reduction in hearing. She was transferred to the emergency ward for observation. Improvement in symptoms was noted within 4 h. After spending the night in the emergency ward, she presented 3 days later in the neurology clinic with complaints of “flashbacks” of diffuse dizziness, apprehension, “heaviness in the legs”, marked memory deficits, and difficulty in concentrating. Physical, neurologic, and mental status examinations found nothing except significant apprehension. The house doctor (M.B.A.) suspected an anaphylactic reaction either to Cyclogyl or to Novesin and referred the patient for allergologic investigation.

Topically applied ophthalmic cyclopentolate can simulate anaphylaxis.

As the absence of conjunctivitis, itching, erythema, urticaria, bronchospasm, etc. was not typical of an immune-mediated anaphylactic reaction, the Swiss Drug Monitoring Center, Chur, Switzerland (M.K.), and the manufacturer of Cyclogyl eye-drops (Alcon Pharmaceutical Ltd) (B.Z.M.) were asked for a comment.

Cyclopentolate is widely used in ophthalmology for its intense mydriatic and cycloplegic activity. Systemic side-effects, mainly cerebellar or cerebral, such as visual and tactile hallucinations, incoherent speech, agitation, disorientation, memory loss, and acute psychotic reactions, have been described after topical administration of ocular cyclopentolate. These reactions appear to be dose-related and are more common in children, with high concentrations or high doses, but have been reported rarely in adults receiving normal doses (2–5). The onset ranges from 20 min to 1 h, and the reactions are generally transient.

Little is known about the metabolism of cyclopentolate (5). It is rapidly adsorbed into the systemic circulation, after ocular administration (6), through the cornea, conjunctiva, nasal mucosa, and gastrointestinal (GI) tract. A second peak at 2–4 h observed in some subjects may reflect GI adsorption from drug swallowed after drainage into the nasopharynx through the nasolacrimal duct. Drug drainage from the eye to the main site of unwanted adsorption, the nose, is increased by a large volume and/or multiple drops. Blinking also accelerates the transit of eye-drops from the conjunctival sac to the nose. Careful instillation of a drop, followed by eyelid closure and nasolacrimal occlusion, may increase the retention of the drug in the eye. Lid closure reduces the action of the nasolacrimal pump. Prolonged eye–drug contact may increase the desired ocular effect, while obstructing drainage to the nasopharyngeal mucosa might decrease the

amount of drug in the circulatory system, decreasing systemic side-effects.

According to the Product Safety Department of Alcon Laboratories (SP, Fort Worth, TX, USA), our patient appears to have experienced systemic pharmacologic effects after instillation of 1% cyclopentolate. Although the ophthalmologist felt that much of the instilled product was wiped away, our patient may have adsorbed more than expected. She also received oxybuprocaine, an ester local anesthetic, which may have contributed to her reaction. Restlessness, dizziness, tinnitus, blurred vision, and nausea are possible adverse events associated with local anesthetics.

In conclusion, beside allergic reactions to components in eye-drops (1, 7, 8), the allergologist should also consider systemic pharmacologic side-effects due to abnormally high drug absorption at the receptor site or increased receptor sensitivity in some individuals.

*Allergy Unit
Department of Dermatology
University Hospital Zurich
Gloriastrasse 31
CH-8091 Zurich
Switzerland
Fax: +41-1-255 44 31
E-mail: wuetric@derm.unizh.ch

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