

Oral azithromycin combined with topical anti-inflammatory agents in the treatment of blepharokeratoconjunctivitis in children

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We report 3 children referred for recurrent blepharokeratoconjunctivitis, despite topical antibiotic and anti-inflammatory treatments. Oral azithromycin combined with anti-inflammatory treatment was effective in controlling the disease.

Blepharokeratoconjunctivitis (BKC) can lead to significant ocular discomfort, recurring chalazia, conjunctival/corneal phlyctenules with secondary neovascularization and scarring.¹ These changes in children may compromise visual acuity and lead to amblyopia.²

Case 1

A 30-month old Hispanic boy presented to the Illinois Ear and Eye Infirmary with blepharokeratoconjunctivitis. He had recurrent bilateral chalazia since 9 months of age and a corneal ulcer in the left eye at 20 months. Previous treatment included loteprednol, artificial tears, and bacitracin ointment. Examination showed bilateral eyelid scurf and meibomian gland plugging. The right eye had an upper lid chalazion, and the left eye had a temporal perilimbal phlyctenule with neovascularization 5 mm in diameter. The patient was initially treated with lid hygiene, topical loteprednol 0.2% (Alrex; Bausch & Lomb, Rochester, NY) 3 times daily in the left eye, and oral azithromycin 100 mg daily (5 mg/kg daily).

At 1 month follow-up the patient had decreased photophobia but a persistent phlyctenule. Treatment continued for an additional 6 weeks, with reduction in inflammation and vascularization of the phlyctenule. Loteprednol was slowly discontinued, Azithromycin was reduced to every other day, and cyclosporine ophthalmic drops, 0.05% (Restasis; Allergan, Irvine, CA), twice daily, were added to the left eye.

Ten weeks later, 4 weeks after running out of his medications, the patient returned

with left eye discomfort and hyperemia. Examination showed injection and corneal opacification in his left eye. He was again started on loteprednol drops 3 times daily in the left eye. tapered off over 3 weeks, cyclosporine ophthalmic drops twice daily in the left eye, and oral azithromycin 100 mg daily for 2 months. At follow-up 4 and 10 months later, he had no eye complaints and examination showed a small corneal scar in the left eye, with no signs of active phlyctenulosis.

Case 2

An 8-year-old boy with a history of BKC and a right corneal scar since the age of 3 years was referred for bilateral photophobia, redness, and itchiness. Topical steroids and antibiotics had been used as previous treatments. Visual acuity with correction was measured as 20/125 in the right eye and 20/60 -2 in the left eye. Examination revealed bilateral blepharitis with a large central scar with neovascularization and a perilimbal scar in the right cornea. The left cornea had scattered stromal infiltrates and lower peripheral punctate epithelial erosions. Lid hygiene, cyclosporine drops, 0.05%, 4 times daily to the right eye, and oral azithromycin 160 mg daily (5mg/kg daily) were prescribed. His previously prescribed prednisolone ophthalmic drops 4 times daily were tapered down over 3 weeks.

Three weeks later the patient had no photophobia, redness, or itchiness. His best-corrected visual acuity had improved to 20/60 +2 in the right eye and 20/30 -2 in the left eye. Examination showed regression of the right corneal central and perilimbal scars. The left eye had a reduction in scattered stromal infiltrates and punctate epithelial erosions. Treatment continued with oral azithromycin 160 mg daily for an additional 3 weeks then every other day for 1 more month. Cyclosporine was reduced to 3 times daily over this

time period. At 6 months' follow-up, his symptoms remained under control, with only occasional redness. Visual acuity with correction was 20/125 -1 in the right eye and 20/25 in the left eye. Examination showed phlyctenular scars with no active vessels in the right cornea and a few punctate epithelial erosions in the lower periphery of the left cornea.

Case 3

A 4-year-old boy with a 1-year history of bilateral keratitis and left corneal scarring was referred to our clinic. The patient had been diagnosed with keratitis 18 months earlier and had been treated with neomycin-polymyxin b-dexamethasone ophthalmic, with temporary relief. The patient was patching the right eye 3 hours daily, given concern for amblyopia. On ophthalmological examination, the patient had an uncorrected visual acuity of 20/160 in the right eye and 20/320 in the left eye. He had moderate blepharitis with meibomian gland dysfunction bilaterally. Mild central stromal haze was noted in the right cornea. In the left eye, a central corneal scar with stromal haze as well as phlyctenule infiltrates on the inferior margins of the cornea were observed. The patient was started on oral azithromycin 80 mg daily (5 mg/kg daily) and cyclosporine drops, 0.05%, to both eyes 3 times daily.

At 1 month follow-up, ocular discomfort and photophobia had decreased. Visual acuity improved to 20/40 in the right eye and 20/200 in the left eye. A central corneal scar and stromal haze remained in the left eye but no phlyctenular infiltrates were noted. The patient was continued on his regimen of oral azithromycin and cyclosporine drops for another month and referred to the pediatric ophthalmology clinic for amblyopia management. At 21 months' follow-up, the patient was no longer on any ocular or

systemic medication. Visual acuity without correction had improved to 20/25 in the right eye and 20/50 in the left eye. The right eye had scattered stromal opacities, and the central scar and stromal haze in the left eye persisted.

Discussion

Blepharokeratoconjunctivitis is underdiagnosed in children.³ A stepwise approach to treatment begins with lid hygiene followed by topical antibiotics such as erythromycin or bacitracin ointments.⁴ If still present oral doxycycline is used in adults, but its side effects in children, most notably tooth discoloration, restrict its use.⁵

In children, oral erythromycin therapy is a proven and effective option; however, it needs to be dosed multiple times daily.⁶ As an alternative, we examined oral azithromycin. Whereas oral azithromycin is reported to be effective in the treatment of posterior blepharitis in adults, the data on its use in children is limited.⁷ While having the same mechanism of action as erythromycin, azithromycin has improved oral bioavailability, longer half-life (allowing once daily dosing), higher tissue concentrations, enhanced microbial activity, and reduced gastrointestinal side effects⁸: the most common macrolide side effects are experienced half as often with azithromycin.⁹ The cost of an erythromycin regimen (150 mg daily) of 8 months duration is approximately \$400 whereas an azithromycin regimen (125 mg daily) for 3 months may cost twice as much.

While further studies are needed, these 3 cases suggest a positive effect of oral azithromycin in the treatment of persistent BKC in children. Given the inflammatory nature of the disease, we combine azithromycin with anti-inflammatory therapy using short-term steroids and long-term cyclosporine drops. Although this combined therapy clouds the exact effect of oral azithromycin, given its simpler dosing and better

tolerance, azithromycin appears to be a possible substitute for oral erythromycin in persistent BKC.

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