

Emerging fluoroquinolone resistance in bacterial keratitis

Alvin L. Young, FRCS, Gloria Y. S. Leung, MBBS, Alfred T. S. Leung, FRCS, Dennis S. C. Lam, FRCS, FRCOphth
Department of Ophthalmology & Visual Sciences, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong, China.

Dear Editor,

In Hong Kong, bacterial keratitis is a common problem encountered by ophthalmologists. Infectious patients may initially present to private ophthalmologists and treatment with a broad-spectrum antibiotic as empirical therapy is commenced.¹

Since the introduction of ofloxacin in 1993, there has been rapid acceptance of ciprofloxacin and ofloxacin due to the broad-spectrum activity against gram-negative and many gram-positive organisms, including *Pseudomonas* and *Staphylococcus* species. These agents are favored since they are commercially available and are stable at room temperature. In addition, studies have reported that ofloxacin monotherapy for the primary treatment of microbial keratitis is as equivalent in terms of healing as the fortified regimens, for example tobramycin-cefazolin.²⁻⁴

As a tertiary referral center, we encountered 2 patients with ofloxacin-resistant microbial keratitis in June 2001, accounting for approximately 20% of the patients with microbial keratitis seen during March 2001 to June 2001.

Case 1

A 29-year-old man sustained a non-specific foreign body injury to his left eye 3 days before presentation. The foreign body was allegedly removed by his colleagues with folded paper. On examination, he was found to have a para-axial corneal ulcer associated with a dense white infiltrate. The patient was given hourly topical ofloxacin after corneal scraping was performed. Only white blood cells were seen on microscopy with a negative gram stain. There was very little improvement after 24 hours of intensive topical therapy with the development of a hypopyon. Subsequent culture results yielded *P aeruginosa* and sensitivity tests were found to be insensitive to ofloxacin. A combination of fortified topical ceftazidime 50 mg/ml and tobramycin 15 mg/ml was commenced at 2-hourly intervals. Recovery was uneventful and the epithelial defect healed after 48 hours of treatment.

Case 2

A 21-year-old man presented with a 2-day history of a red painful left eye. He had used soft contact lenses for the previous 2 months. On examination, he was found to have a para-axial ulcer associated with an infiltrate and a 1 mm hypopyon. The patient was given hourly topical ofloxacin and fortified topical ceftazidime 50 mg/ml after scraping was performed. A large number of white blood cells were seen on microscopy together with a large number of gram-negative bacilli.

After 3 days of intensive antibiotic application, the hypopyon cleared, although the size of the infiltrate remained static. Sensitivity testing revealed a heavy growth of *P aeruginosa* that was resistant to ofloxacin. Fortified topical tobramycin 15 mg/ml was substituted for ofloxacin. There was marked improvement after 1 day of therapy, with gradual healing of the epithelial defect and subsequent uneventful recovery.

Comment

For many years, antibiotic resistance has been of increasing concern.^{5,6} During the 1990s, many studies reported an increasing degree of resistance of ocular isolates to fluoroquinolones, especially for *S aureus* and *P aeruginosa*.⁷ Resistance rates of *S aureus* to ciprofloxacin and ofloxacin in Pittsburgh increased by 5 to 35% between 1993 and 1997,^{8,9} while the rate of resistance of *P aeruginosa* to ciprofloxacin rose significantly from 0.4% during 1991 to 1994 to 4% during 1995 to 1998 in Florida.^{10,11} Similar increases in ciprofloxacin resistant gram-positive cocci and *P aeruginosa* have been reported in India.¹² These data support discontinuing rather than tapering topical multidose antibiotic therapy, contrary to the accustomed practice of ophthalmologists.

In summary, resistance rates of ocular isolates to aminoglycosides and quinolones are increasing in many areas of the world.¹¹ The local ophthalmic community should be alerted to an over-reliance on fluoroquinolones for severe

ocular infections, and its injudicious use as a 'prophylactic' agent is probably not desirable. In a tertiary referral center, evaluation with microbiologic studies is crucial, even if the patients have already commenced antibiotics prior to referral.

Recognition of culture-tested sensitivities and prudent use of antibiotics are essential to successful treatment and, hopefully, a reduction in the local emergence of resistant pathogens.

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