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CEED²: Confronting the 'Silent Epidemic'

An overview of corneal infections and antibiotics in Asia

Corneal blindness in the Asia-Pacific region is so significant it has been called a "silent epidemic," said **Donald Tan, MD**, medical director, Singapore National Eye Centre, Singapore, kicking off the 2nd Cornea and External Eye Disease (CEED²) Advisory Board Meeting by Bausch + Lomb (Rochester, NY, USA), which preceded the Asia Cornea Society's 3rd Biennial Scientific Meeting held in Manila, Philippines, in November 2012.

Prof. Tan was one of an impressive panel of experts and key opinion leaders from around the region and the United States brought together for CEED² with the aim of reviewing practice patterns and factors influencing the management of ocular infections, identifying current management gaps, and exploring the entire treatment landscape in the region, particularly in light of the (at the time) pending introduction of Besivance (besifloxacin 0.6% ophthalmic suspension, Bausch + Lomb), a new topical antibiotic agent available exclusively for ophthalmic use.

Focus: Asia

Why focus on Asia? Prof. Tan quoted an oft-cited paper written by John Whitcher,[1] that called corneal ulceration a "silent epidemic" in the region—second only to cataract in overall importance as a cause of blindness.

Most cases of corneal blindness, said Prof. Tan, occur "in Asia and Africa, not elsewhere."

But the challenge of corneal blindness in Asia isn't confined to magnitude. Unsurprising to anyone familiar with the region, huge variations exist from country to country, such that the problem runs the gamut of the spectrum of corneal infections.

"Trauma, ulceration of the cornea, and infections are really significant causes, and this is not even including monocular cases," said Prof. Tan, adding that the challenges have to do with having "different bugs, different drugs" in any given part of the region.

Citing one example of the wide variation seen in the region, Prof. Tan noted how contact lens use has been identified as a major risk factor for ocular surface infections in countries like Japan (54.5%),[2] Singapore (34%),[3] and Taiwan (44.3%),[4] but was associated with only 0.56% of cases in South India.[5]

"Even the microbiology is different," he said. "*Pseudomonas* is the commonest cause of contact lens-related keratitis [e.g., 86% in Hong Kong,[6] 79% in Singapore[3]], but in Japan, [54.5%[7]] of all cases of contact lens-induced keratitis are gram positive."

Elsewhere, fungal keratitis comprises significant percentages of cases. In fact, Prof. Tan said that fungi are the most common pathogen for infectious keratitis in Asia, although the particular species again varies by geographic region.

Parasitic keratitis is also a significant problem in some areas, while Prof. Tan expects to see more otherwise healthy patients (as opposed to the immunocompromised or immunosuppressed patients typically seen in previous decades) diagnosed with microsporidial keratitis.

Antibiotic use also varies widely, with practices not typically being evidence-based. Some countries in what Prof. Tan called the "chloramphenicol group" (including Hong Kong, Malaysia, and Thailand) follow antibiotic use practices established by British colonists (practices which, he added, were not used in the United States), whereas elsewhere in the region, there is simply "no real pattern."

Basically, he said, the dictum guiding medical management in the region is "we use what we can," whether drugs are available over-the-counter, prescribed by ophthalmologists, primary care physicians, or even pharmacies, and provided with or without government subsidy.

Significantly, knowledge of local resistance patterns is variable—often sparse—as is access to primary eyecare and to the latest antibiotics. "We know from the West that bacterial isolates from infections have been increasing in resistance," he said, citing results from the Ocular TRUST study.[8] "Is this relevant to Asia? We need to find the answers."

There are "a few good antibiotic surveillance studies"—such as TRUST, PROTECT, SENTRY, and ARMOR, to name a few—"but they're mostly in the West—Canada, Latin America, Europe, [historically] none in Asia," Prof. Tan said.

One of the few good studies from the region, conducted in Taiwan and looking at a 10-year period, reported a distressingly high rate of methicillin resistance among patients with *Staphylococcus aureus* infections—52.8%, "the largest reported case series ever for ocular MRSA [methicillin-resistant *S. aureus*]," said Prof. Tan.[9]

The crux, said Prof. Tan, is that for the region, "we need to know the bugs," he said. "We need to know the resistance patterns. We need to come up with evidence-based antibiotic regimens. We need to do clinical trials properly."

To that end, the Asia Cornea Society (ACS), currently presided over by Prof. Tan, has embarked on the ACS Infectious Keratitis Study (ACSIKS), a multicenter, prospective observational study in 11 study centers in eight major locations (China, India, Japan, Korea, Philippines, Taiwan, Thailand, and Singapore).

The study is intended to document the clinical management practices of doctors all over the region, while also collecting microbiological samples from recruited cases.

The India variations

As an example of one significant variant in epidemiological pattern in the Asia-Pacific region, **Prashant Garg, MD**, director, education, and consultant ophthalmologist, cornea and anterior segment, LV Prasad Eye Institute, Hyderabad, India, shared some information on the situation in his country.

According to Dr. Garg, "classical diseases" such as trachoma, onchocerciasis, leprosy, ophthalmia neonato-

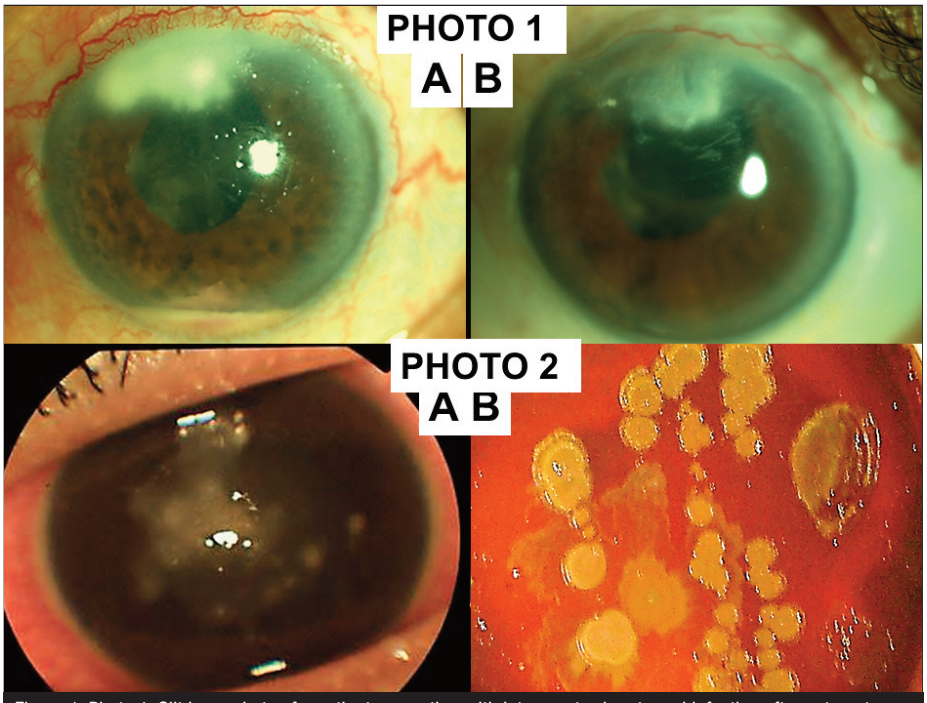


Figure 1. Photo 1: Slit lamp photo of a patient presenting with late onset sclera tunnel infection after cataract surgery (A) and after treatment (B). Photo 2: Slit lamp photo of a patient with *S. aureus* infection after CXL treatment with atypical multifocal infiltrate presentation (A). The culture plate shows typical golden yellow colonies on blood agar (B).

Source: Anand Parthasarathy, MD

rum, and xerophthalmia that were initially responsible for much blindness in the developing world have already come under control in the last few decades thanks to "effective public health interventions" such as vitamin A supplementation.

This has led Dr. Garg and his colleagues to shift their attention onto other conditions. "Some of the other groups of diseases are becoming more of a concern," particularly corneal infections—keratitis in both children and adults—trauma, and the widespread use of harmful eye practices including certain unsubstantiated folk remedies, he said.

"If you look at the data published from various developing countries on the incidence of corneal infections"—including reports published in the *British Journal of Ophthalmology* and national statistics data from countries like Bhutan and Myanmar—"it is estimated that nearly 1.5 to 8 million corneal infections occur each year in the developing world," he said. It was this data, he said, that led John Whitcher and M. Srinivasan to call corneal infection a "silent epidemic."[1]

Analyzing data gathered over the last 10 years, Dr. Garg and his colleagues found that almost half of patients were managed inappropriately. Many of these patients were using combinations of antibiotic and corticosteroid before being referred to a tertiary eyecare center.

"We are very good at using drugs as soon as we are convinced that they are good and they become available," said Dr. Garg. For instance, the various generations of fluoroquinolone are used for a variety of indications including the first-line treatment of keratitis and prophylaxis against postoperative endophthalmitis. Furthermore, these drugs are also used widely not only in ophthalmology but also systemically for other systemic medical conditions, in poultry and for infections in animals.

The results, he said, are alarming.

In 2002, minimum inhibitory concentrations (MICs) of moxifloxacin and gatifloxacin even for ciprofloxacin-resistant gram-positive organisms were very low, although they were equally high for *Pseudomonas* and other gram-negative infections. By 2009, when Dr. Garg and his colleagues analyzed the data, half of the organisms were already resistant to moxifloxacin, about a quarter resistant to gatifloxacin.

An even more worrying phenomenon is the increasing proportions of keratitis isolates of *Pseudomonas*, which show resistance not only to fluoroquinolones but to other antimicrobial agents, a problem parallel to methicillin resistance among gram-positive organisms.

"We currently have a serious problem of multidrug-resistant *Pseudomonas*," he said.

The challenges faced by ophthalmologists in managing corneal infection in India are unique but also apply to many developing nations in the Asia-Pacific region: An unexpectedly high number of young adults suffer from the problem, and most ophthalmologists do not have access to microbiological facilities and therefore treat patients empirically with a combination of antimicrobials to provide broad-spectrum coverage. To prevent blindness from this disease, Dr. Garg stressed the need to educate the public against the use of homemade remedies and other harmful practices while educating healthcare providers in early diagnosis, appropriate treatment, and timely referral to tertiary eyecare centers.

Managing atypical presentations of corneal infections

One consequence of the situation in developing countries is that patients may (and often do) present atypically or with atypical infections. These atypical cases, said **Anand Parthasarathy, MD**, chief medical officer and head, corneal service, Vasan Eye Care Hospitals, India, present significant diagnostic and therapeutic challenges to physicians.

In South Asia and other developing countries, trauma is a major contributing factor in initiating infections. This, however, might not always be elicited. In the Asian context, infective etiologies are more likely causes of corneal lesions; hence, steroids need to be used with extreme caution in cases where an immune-mediated keratitis is presumed.

Postop infections are a category of cases that may present atypically. While sutureless large incision cataract surgery (SICS) is commonly performed in Asia with good visual results, these incisions can occasionally get infected. Dr. Parthasarathy presented a case of a doctor who had undergone SICS surgery and developed late onset sclera tunnel infection that did not respond to newer antibiotics (Figure 1, photo 1A). Corneal biopsy revealed atypical mycobacterium (*Mycobacterium massiliense*) identified with DNA typing—an organism that has rarely been reported from ocular isolates (article in submission). The case was treated with topical clarithromycin 1% and amikacin 2.5%, leading to resolution of infection (Figure 1, photo 1B).

Postop patients, those who have undergone laser keratomileusis or surface ablation, are at risk of infection

from gram positives or atypical mycobacteria. Meanwhile, newer procedures such as corneal crosslinking cause changes in the corneal stromal architecture and immune responses that may lead to an unusual morphology of infections; Dr. Parthasarathy presented a case of post-CXL infection (Figure 1, photo 2A) for whom *Staphylococcus aureus* was isolated in culture (Figure 1, photo 2B) who did not have the commonly described clinical picture. Furthermore, since corneal crosslinking is performed for keratoconus, postop infections need to be treated aggressively since stromalysis leading to perforation can occur.

According to Dr. Parthasarathy, present evidence indicates that prophylaxis with newer fluoroquinolones provides adequate coverage in patients undergoing corneal and intraocular surgery, although atypical mycobacterial infections require additional agents.

In any case, he added, treatment of infections should be guided by sensitivity patterns appropriate to the region of practice, especially in cases with atypical presentation.

Understanding the science

Setting aside the nuances of practice in any region of the world, the obvious lynchpin of medical management in cases of corneal infection remains the availability of effective antimicrobial agents. **Penny Asbell, MD**, professor of ophthalmology, Mount Sinai School of Medicine, NY, USA, looked at some pharmacological concepts useful when considering the effectiveness of antibiotics in the laboratory.

According to Dr. Asbell, you need to think about "at least three factors together" when talking about antibiotics: the drug itself, the target organism, and target tissue—in the laboratory setting, this is the culture media.

Pharmacologically, Dr. Asbell revisited a few key concepts: minimum inhibitory concentration (MIC) and inhibitory quotient (IQ).

Minimal inhibitory concentration

The minimal inhibitory concentration (MIC) is the conventional measure for assessing bactericidal efficacy of antimicrobial agents, including those for ocular infections. Comparative MIC data are expressed in terms of the MIC_{50} (the concentration necessary to fully inhibit growth of ≥50% of at least six independent isolates) and the MIC_{90} (the concentration necessary to fully inhibit growth of ≥90% of at least 10 independent isolates).

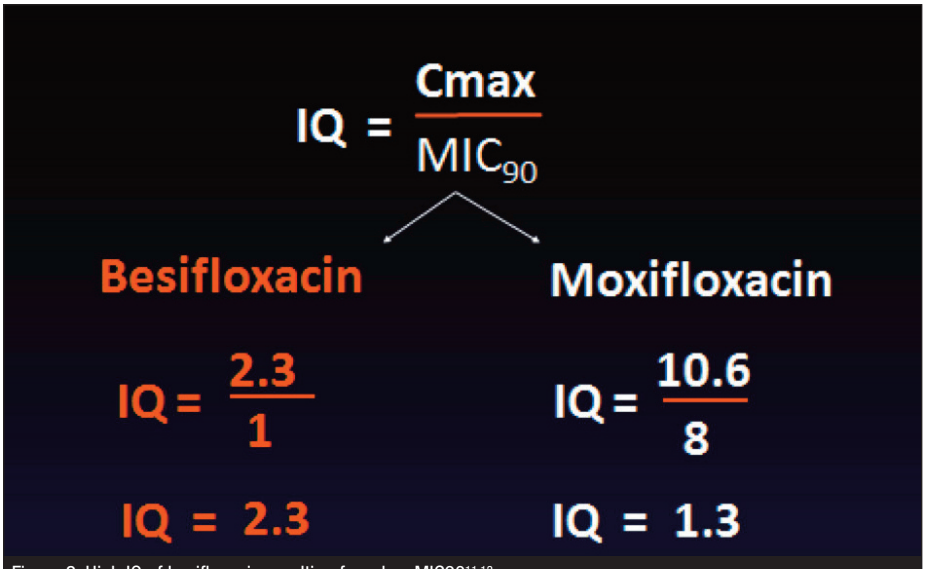
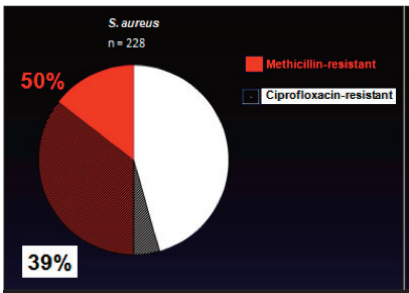


Figure 2. High IQ of besifloxacin resulting from low MIC90[11,12]

Source: Penny Asbell, MD



Antibiotic	MIC Range	MIC_{50}	MIC_{90}
Vancomycin	≤0.25 – 2	0.5	1
Besifloxacin	≤0.008 – 4	0.03	1
Moxifloxacin	0.008 – 64	0.06	8
Gatifloxacin	0.03 – 256	0.12	8
Ciprofloxacin	0.016 – 512	0.5	256
Tobramycin	≤0.06 – >256	0.5	256
Azithromycin	≤0.25 – >512	128	>512

Figure 3. ARMOR 2010: MICs against all *S. aureus* (including methicillin- and ciprofloxacin-resistant strains as indicated by the pie char)[13]

Source: Haas W, et al. 2010

	Besifloxacin	Moxifloxacin	Gatifloxacin
$AUC_{0\text{-}24}$ (μg.hr/mL)	6.65	11.12	6.10
MRT (hrs)	4.70	2.99	2.92
C_{max} (μg.g)	2.30±1.42	10.60±1.40	4.30±3.84

Table 1. Concentrations of besifloxacin in human conjunctiva[12] ; AUC: Area under the curve from 0 to 24 hours; MRT: Mean residence time; C_{max}: Maximum plasma concentration

Source: Torkildsen G, et al. 2010

The newest member of the fluoroquinolone family, besifloxacin, demonstrates better clinical efficacy than its older counterparts. Against ciprofloxacin-resistant *Staphylococcus aureus*, besifloxacin has shown high in vitro potency with a lower MIC than other fluoroquinolones, including moxifloxacin and gatifloxacin.[10] Besides *S. aureus*, other common ocular pathogens, such as methicillin-resistant *S. aureus* (MRSA), *Staphylococcus epidermidis* (including methicillin-resistant strains [MRSE]), *S. pneumoniae*, and *Haemophilus influenza*—including isolates that are resistant to other fluoroquinolones—are susceptible to besifloxacin, as determined by comparison of MICs.[10]

Inhibitory quotient

Compared with MIC, a more comprehensive predictor of antibiotic efficacy is the inhibitory quotient (IQ), which combines measures of potency with the concentration of the drug in the relevant tissue. The IQ is the maximum concentration (C_{max}) of a given drug divided by its MIC_{90} after application of one dose. One study comparing the conjunctival IQs of the newest fluoroquinolones against *S. aureus* ocular isolates showed besifloxacin had an IQ of 2.3, and moxifloxacin an IQ of 1.3.[11,12] Although besifloxacin achieves lower tissue concentrations, it also has a lower MIC_{90}, resulting in a higher IQ (Figure 2).

Changing pattern of antibiotic susceptibility

Ocular pathogen resistance to antimicrobial agents is increasing in parallel with an increase in antibiotic resistance in general and presents a major clinical challenge, as shown in the TRUST studies.[8] The recent Antibiotic Resistance Monitoring in Ocular Micro-organisms (ARMOR) surveillance study showed that a significant fraction of ocular isolates are becoming resistant to one or more of commonly used antibiotics. The results indicated that 50% of *S. aureus* ocular isolates were methicillin-resistant, 39% were ciprofloxacin-resistant, and 36% were resistant to both.[13] Of the coagulase-negative *Staphylococci* isolates, 57% were methicillin-resistant, 39% were ciprofloxacin-resistant, and 34% were resistant to both (Figure 3).[13]

Among the antibiotics studied in the ARMOR, vancomycin and besifloxacin had the lowest MIC_{50} and MIC_{90} for all *S. aureus* isolates, each with an MIC_{90} of 1, compared to 8 for moxifloxacin and 256 or higher for ciprofloxacin and the non-fluoroquinolones (Figure 3).[13]

Community-acquired MRSA on the rise

Alarmingly, ocular MRSA isolates now include substantial proportions of both hospital and community strains.[14] Although community-acquired MRSA is generally easier to treat compared with hospital-acquired strains, it is becoming more virulent and increasingly more multidrug-resistant even in the ocular setting. Therefore, surveillance studies are important for tracking trends of susceptibility among ocular pathogens and providing clinicians a starting point for drug selection.

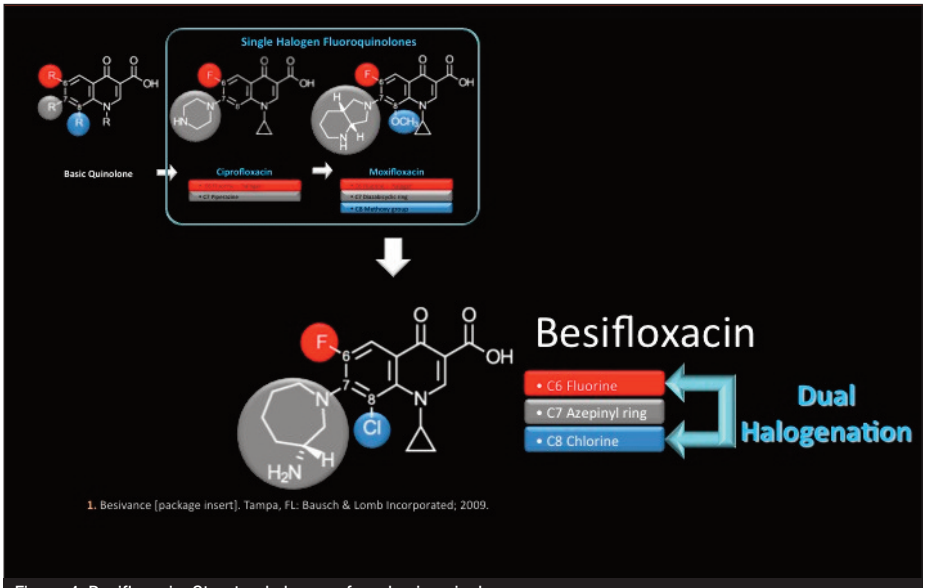


Figure 4. Besifloxacin: Structural changes from basic quinolone
Source: Besivance [package insert]. Tampa, Fla., US: Bausch + Lomb Incorporated; 2009

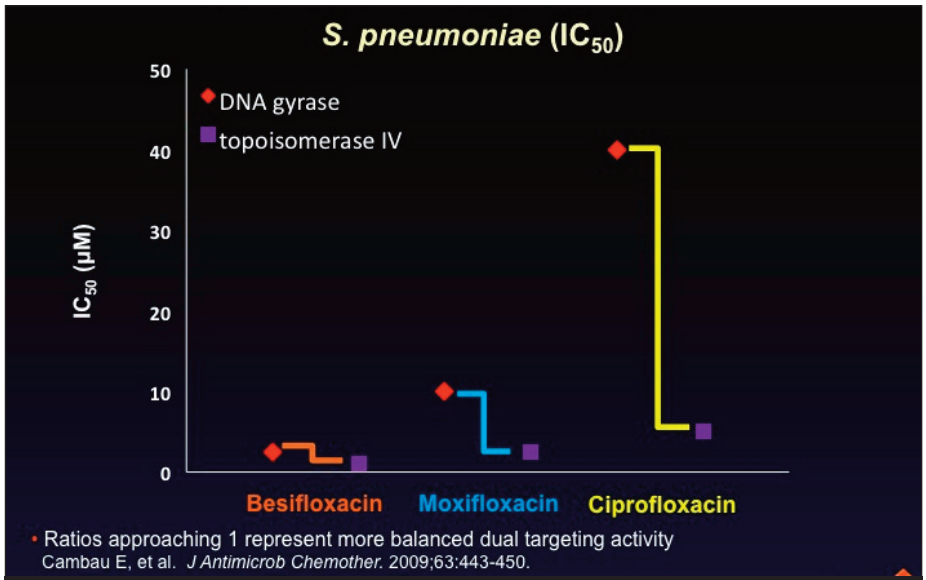


Figure 5. Comparison of DNA gyrase and topoisomerase inhibition between besifloxacin, moxifloxacin, and ciprofloxacin showing balanced and potent inhibition of the two essential bacterial enzymes with besifloxacin
Source: Cambau E et al. 2009

Introducing besifloxacin, the only chlorofluoroquinolone

Besifloxacin is a new chemical entity of fluoroquinolone, with a unique chlorine substituent at the C8 position of the quinolone ring providing a different antimicrobial profile (Figure 4).[15] The polycarbophil-based vehicle DuraSite® prolongs the drug's residence time on the ocular surface and increases its bioavailability.[16] Even 12 hours after administration of a single drop, the tear concentration of besifloxacin is sustained above the MIC values observed for all susceptible bacterial pathogens.

Besifloxacin's mechanism of action is consistent with other fluoroquinolones in that it inhibits both DNA gyrase and topoisomerase IV enzymes. Different fluoroquinolones interfere with these enzymes to varying degrees—ciprofloxacin has been called a single-mechanism fluoroquinolone for potently inhibiting topoisomerase IV without much of an effect on DNA gyrase. Later dual-mechanism fluoroquinolones such as moxifloxacin—and now besifloxacin—add potent DNA gyrase inhibition to the equation.

What besifloxacin improves upon over older fluoroquinolones like moxifloxacin and gatifloxacin in terms of mechanism of action is a better balance between the two mechanisms of action: The active ingredient inhibits one enzyme as potently as the other (Figure 5).[17] This agent has been developed exclusively for ophthalmic use and has no systemic counterparts, thus further minimizing resistance to the drug over the long term.

Besifloxacin has been indicated for use against a broad range of bacteria, including *Staphylococcus*, *Streptococcus* and *Corynebacterium* species. In addition to gram-positive bacteria, besifloxacin has also shown efficacy in treating infections caused by gram-negative bacteria, such as *Moraxella* species and *H. influenza*.

Lower MIC, more potency in vitro

Compared with other fluoroquinolones, besifloxacin has demonstrated greater potency when assessed in gram-positive pathogens, including methicillin-resistant and fluoroquinolone-resistant *S. aureus* and *S. epidermidis*.[10,18] Although the MICs increase with the number of mutations that confer fluoroquinolone resistance,

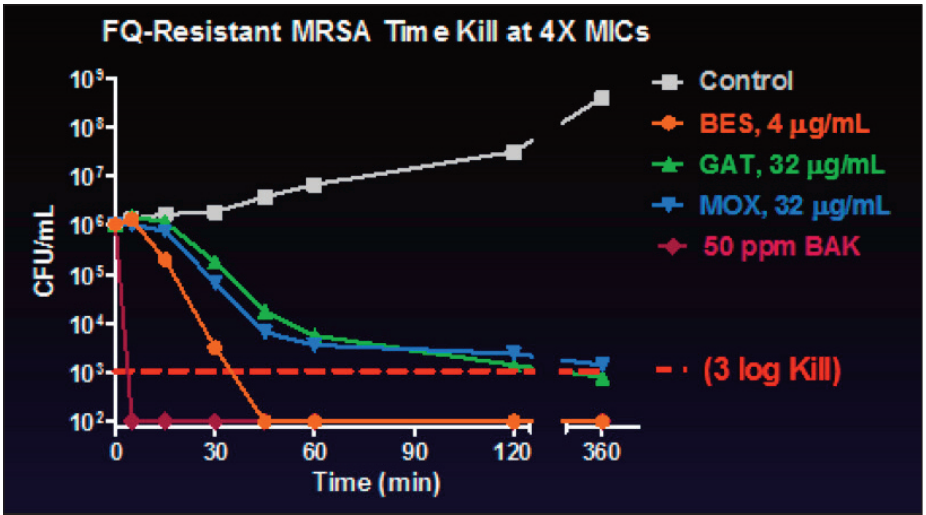


Figure 6. Besifloxacin kills faster than gatifloxacin or moxifloxacin[23]

Source: Haas W, et al. 2009

this increase is found to be the smallest for besifloxacin and the largest for ciprofloxacin and levofloxacin.[19]

Higher IQ, more efficacy in vivo

The very high potency (i.e., low MIC_{90} values) of besifloxacin against clinically important pathogens results in a high IQ even though tissue concentrations may not be as high as those for other fluoroquinolones. The IQs of besifloxacin are consistently higher than those of the other fluoroquinolones in the tears, conjunctiva, cornea, and aqueous humour.[20] However, low penetration in the anterior chamber remains a limitation common to all members of the fluoroquinolone family.[21]

Fastest speed of kill

There is controversy around the role of the preservative benzalkonium chloride (BAK) in bacterial eradication. In vitro, BAK tends to enhance kill speed, but since the preservative dissipates rapidly from human tears,[22] the active drug is the more important determinant of the speed-kill curve in vivo. In vehicle-controlled bacterial conjunctivitis trials, BAK-containing vehicles consistently underperformed active drugs.

With the speed of bacterial killing measured using physiologically relevant concentrations of active drugs and adjusted for relative MIC differences, besifloxacin has more rapid killing of MSSA and MRSA (both fluoroquinolone-sensitive and resistant strains) than either gatifloxacin or moxifloxacin (Figure 6).[23] A similar kill-rate pattern is seen against *S. epidermidis*.

Safety, power, compliance

Jai G. Parekh, MD, MBA, managing partner, Brar-Parekh Eye Associates, NJ, and clinical associate professor, New York Eye & Ear Infirmary, NY, USA, has used Besivance since 2009. Besivance is the only fluoroquinolone formulation to include the DuraSite vehicle, which helps foster better drug delivery and tissue interaction at the level of the ocular surface. He shared the results of three studies published that year, which provided the data that encouraged him to use besifloxacin: Tepedino et al.[24] and Karpecki et al.,[25] which compared Besivance with vehicle; and McDonald et al.,[26] which compared Besivance with Vigamox (moxifloxacin HCl ophthalmic solution, Alcon, Fort Worth, Texas, US/Hünenberg, Switzerland).

Both the Tepedino and Karpecki studies showed clear antimicrobial activity compared with vehicle, with the Tepedino study additionally noting that fewer adverse events were associated with Besivance compared with vehicle (9.2% vs. 13.9%, respectively, P=0.0047).

Meanwhile, Besivance and Vigamox provided equally high rates of microbial eradication, with adverse events at similar cumulative frequency (12% vs. 14%, respectively).

The most frequently reported ocular adverse event in more 1,000 patients aged 1 to 98 years with clinical signs and symptoms of bacterial conjunctivitis exposed to Besivance was conjunctival redness (~2%). Other events reported (~1-2%) include blurred vision, eye pain, eye irritation, eye pruritus, and headache.[27]

In the end, whatever the trial data may show, "it all boils down to taking care of the patient," said Dr. Parekh. "We want the best outcomes for our patients. When it comes time to treat a patient who has an infection or help prevent the risk of infection, there are several variables that we look at, clinically, day to day, from patient to patient.

"This may also be dosing regimen and compliance, MIC_{90} profiles, and the ability to treat some tougher infections including resistant organisms such as MRSA," he added.

In Dr. Parekh's practice, they have come to use besifloxacin in treating bacterial and mixed conjunctivitis, blepharokeratoconjunctivitis, and bacterial and marginal keratitis. They have also used the drug for perioperative prophylaxis during cataract and LASIK surgery, and have retrospectively examined the safety of Besivance versus Vigamox in these cases as part of a multicenter trial.

The combined data—which included 746 cataract cases (746 eyes)[28] and 801 LASIK cases (801 eyes)[29]—identified no reports of adverse drug reactions related to the antibacterial in either treatment group. In addition, there were no differences between treatment groups in terms of surgical outcomes or distribution of final visual acuity, with most patients having a final VA of 20/20 (6/6) or better.

Dr. Parekh concluded that, in his experience, Besivance was not associated with any unique safety concerns when used in patients undergoing uncomplicated cataract or LASIK surgery.

Friendly regimen

While Besivance is indicated for bacterial conjunctivitis, **John D. Sheppard, MD**, president, Virginia Eye Consultants, Norfolk, VA, USA, has had the opportunity to use the drug in other clinical settings. Like Dr. Parekh, Dr. Sheppard has been using the drug since its introduction in the United States and has been satisfied with the results.

While some of the strategies in which Dr. Sheppard has put Besivance to use are off-label, they serve to illustrate the value of besifloxacin as a new addition to the antibiotic armamentarium.

"Even in the United States, we see a lot of blinding bacterial keratitis," said Dr. Sheppard. "But that still only represents one thousandth the volume of elective ocular surgery. Clearly, the epidemiologic issue is how to apply these antibiotics intelligently to our broadest patient population, that is, the patients undergoing surgery."[30]

At the time of the meeting, Dr.

Sheppard had used Besivance exclusively as prophylaxis in 2,769 surgeries over 41 months, partly in response to the more stringent demand for optimal visual outcomes from patients resulting from, among other things, the introduction of premium IOLs. "Imagine having a disaster in one of these cases," said Dr. Sheppard. "We want to provide our patients with the best possible pharmacological regimen."

In his clinic, Dr. Sheppard uses Besivance twice a day starting the day before surgery (day –1), and up to two weeks after surgery (day +14). The twice daily dosing, he said, increases compliance. "When we used to give TID dosing, that middle-of-the-day dose drove everyone crazy: patients, their families, doctors, and their staff."

In addition to the improved compliance with the twice-daily dosing made possible by Besivance's mucoadhesive DuraSite vehicle, Dr. Sheppard said that the use of the active agent besifloxacin "makes a lot of sense," particularly in light of data from the ARMOR study comparing the MIC_{90}s of besifloxacin with those of moxifloxacin and vancomycin for pathogens typically associated with perioperative infections (e.g., *Strep* and *S. aureus*, including MRSA).[12]

Dr. Sheppard has also been using Besivance as a first-line drug against presumed bacterial keratitis—in this case, in combination with gentamicin. For cases with a presumed bacterial etiology, Dr. Sheppard acquires samples for cultures, injects 0.3 cc (6 mg) gentamicin subconjunctivally (with lidocaine, because, he said, "gentamicin really stings"), and gives besifloxacin drops every two hours (even hours), gentamicin drops every two hours (odd hours), titrating the treatment according to the therapeutic response and the results of culture/sensitivity tests.

"This works very well in our keratitis patients, maybe 60% of whom are contact lens users in Virginia," said Dr. Sheppard.

For infectious keratitis cases, Dr. Sheppard emphasized scrutiny of relevant associations—in his clinic, *Pseudomonas* for all contact lens ulcers, MRSA/MRSE for at-risk patients, protozoans for unresponsive or atypical cases—and culturing prior to treatment, through therapeutic central debridement. Samples from lids and lashes, he said, are "highly correspondent," and the contact lens case can also be sampled "in desperation, when all other sites yield a false negative."

Bugs everywhere

One of the key messages from CEED[2] is that "there are microbes everywhere," said Dr. Sheppard.

"We're all inoculated, all our patients are inoculated," he said. "Bugs do get into the eye, and it's our job to keep them out."

Antibiotics, he said, have been evolving for many years, and the last few have seen tremendous sequential improvements in the vehicle, in MICs, and in IQ with the introduction of besifloxacin.

"With besifloxacin, we have the best next generation fluoroquinolone drop for the eye," he said.

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