Moxifloxacin Treats Resistant Organisms

A study indicates that this agent has the potential to treat *Pseudomonas aeruginosa* and highly resistant *Staphylococcus aureus*.

BY SARA E. SMITH, MANAGING EDITOR

Moxifloxacin (VIGAMOX; Alcon Laboratories, Inc., Fort Worth, TX) is one of the new, fourth-generation fluoroquinolones. A study was performed comparing moxifloxacin 0.5% to vancomycin 50 mg/mL in the treatment of experimental, ciprofloxacin-resistant methicillin-resistant *Staphylococcus aureus* (MRSA) rabbit keratitis, and comparing moxifloxacin 0.5% to ciprofloxacin 0.3% in the treatment of experimental *Pseudomonas aeruginosa* rabbit keratitis. Moxifloxacin proved as effective as the conventional treatment of these highly resistant organisms. Elias Aliprandis, MD, and Harold R. Katz, MD, presented the study's results at the 2003 American Academy of Ophthalmology annual meeting.

"What we are excited about is the fact that this fourth-generation fluoroquinolone has expanded activity against gram-positive organisms and can be used to treat resistant gram-positive organisms," Dr. Aliprandis said during his poster presentation. "Yet, it still maintains excellent in vitro activity against traditional gram-negative organisms that fluoroquinolones are known to treat. It therefore has tremendous potential as monotherapy against numerous organisms that are difficult to treat."

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EXPERIMENTAL MODELS

P. aeruginosa

In one part of the study, investigators sought to determine whether moxifloxacin was equivalent to the "gold standard" in fluoroquinolone treatment of *P. aeruginosa* corneal ulcers: ciprofloxacin. They induced pseudomonas ulcers in the right eye of 25 rabbits. The eyes then remained untreated for 12 hours so that the organisms could replicate. Next, the investigators divided the rabbits into three treatment groups: five rabbits received BSS (Alcon Laboratories, Inc.) as a control, 10 received ciprofloxacin 0.3%, and 10 received moxifloxacin 0.5%.

The investigators administered topical antibiotic therapy at hourly intervals for 12 additional hours. At the end of that time period, they used a standardized method to excise an 8-mm disc of corneal tissue. They then followed standard laboratory techniques to homogenize those tissue samples, place them on solid culture media, and incubate them for 24 to 48 hours. The researchers counted colonies of organisms to determine the quantity of viable bacteria from each rabbit cornea.

Ciprofloxacin-Resistant MRSA Keratitis

In a second arm of the investigation, researchers

TABLE 1. STATISTICAL ANALYSIS OF DIFFERENCES BETWEEN TREATMENT GROUPS IN REDUCING MRSA COLONY COUNTS*

Antibiotic Comparison	Effectiveness**	*P* Value
Moxifloxacin versus control (BSS)	77%	.032
Vancomycin versus control (BSS)	55%	.058
Moxifloxacin versus vancomycin	NA	.552

**Performed using Wilcoxon's rank sum test*

***Percent reduction from control*

induced ciprofloxacin-resistant MRSA keratitis in the right eyes of 25 rabbits. Five rabbits received BSS as a control, 10 rabbits received vancomycin 50 mg/mL, and 10 received moxifloxacin 0.5%. Again, the eyes remained untreated for 12 hours to allow the organisms to replicate.

Topical antibiotic therapy was instituted at hourly intervals for 12 additional hours. At the end of that time period, investigators used a standardized method to excise an 8-mm disc of cornea. They then followed standard laboratory techniques to homogenize those tissue samples, plate them on solid culture media, and incubate them for 24 to 48 hours. The researchers counted colonies of organisms to determine the quantity of viable bacteria from each rabbit cornea.

MOXIFLOXACIN VERSUS CIPROFLOXACIN

Moxifloxacin 0.5% and ciprofloxacin 0.3% were both equivalent in the treatment of *P. aeruginosa* as measured by the reduction in bacterial organisms.

Although the moxifloxacin MIC of the study strain (2.0%) was four times higher than the ciprofloxacin MIC (0.5%), the two drugs performed equally well in the treatment of *P. aeruginosa* keratitis.

Factors contributing to enhanced in vivo moxifloxacin activity against *P. aeruginosa* include greater solubility and better tissue penetration into the cornea than second-generation fluoroquinolones. The investigators concluded that moxifloxacin's favorable pharmacokinetic/pharmacodynamic in vivo profile fully compensates for its reduced in vitro potency against the organism.

MOXIFLOXACIN VERSUS VANCOMYCIN

Both moxifloxacin and vancomycin significantly reduced MRSA colony counts after 12 hours of hourly antibiotic therapy. There were no significant differences in bactericidal activity between the two drugs.

The moxifloxacin MIC was again four times higher than the vancomycin MIC, but the two drugs performed equally well in the treatment of ciprofloxacin-resistant MRSA keratitis.

> "It was a nice surprise to see that you could use [moxifloxacin] to treat a keratitis that is resistant to the earlier generation of fluoroquinolones."

"When you look at the colony counts after 12 hours of therapy, you see that moxifloxacin has as significant treatment effect over control as does vancomycin," Dr. Aliprandis said. "There is no significant difference between vancomycin and moxifloxacin in treating fluoroquinolone-resistant MRSA (resistant to ciprofloxacin, ofloxacin, and levofloxacin). It was a nice surprise to see that you could use this fourth-generation fluoroquinolone to treat a keratitis that is resistant to the earlier generation of fluoroquinolones."

RESULTS

The investigators concluded that, although the MIC of the *S. aureus* used against moxifloxacin is higher than for vancomycin, moxifloxacin has a greater penetration into ocular tissue than the earlier fluoroquinolones. The same holds true for *P. aeruginosa*.

In addition, vancomycin has its disadvantages, according to Dr. Aliprandis, including its time-dependent killing mechanism, which makes vancomycin slower at reducing bacterial counts in the initial hours of treatment. He also stated that vancomycin does not penetrate the cornea as well as moxifloxacin, vancomycin has more epithelial toxicity, and vacomycin is only effective against gram-positive organisms. ■

TABLE 2. STATISTICAL ANALYSIS OF DIFFERENCES BETWEEN TREATMENT GROUPS IN REDUCING *PSEUDOMONAS AERUGINOSA* COLONY COUNTS*

Antibiotic Comparison	Effectiveness**	*P* Value
Ciprofloxacin versus control (BSS)	100%	.0046
Moxifloxacin versus control (BSS)	99.9%	.0069
Moxifloxacin versus ciprofloxacin	NA	.1120

**Performed using Wilcoxon rank sum test*

***Percent reduction from control*

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