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REVIEW

Safety of besifloxacin ophthalmic suspension 0.6% in refractive surgery: a retrospective chart review of post-LASIK patients

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Background: To evaluate the safety of besifloxacin ophthalmic suspension 0.6% when used in laser-assisted in situ keratomileusis (LASIK) prophylactic antibiotic regimens.

Methods: Retrospective surveillance of LASIK surgery cases where besifloxacin ophthalmic suspension 0.6% or moxifloxacin ophthalmic solution 0.5% were prescribed as prophylactic medications. Surgeons from nine US surgical centers provided retrospective case information on surgical outcomes from consecutive cases and reported any adverse events related to the antibacterial used. The primary endpoint was the incidence of adverse drug reactions.

Results: A total of 801 case reports (801 eyes; 534 besifloxacin, 267 moxifloxacin) were obtained. The mean (standard deviation [SD]) age at time of surgery was 36.1 (10.6) years. The mean (SD) duration of antibiotic treatment was 8.6 (2.2) days in the besifloxacin group and 8.0 (2.3) in the moxifloxacin group; daily dosing frequency was higher in the moxifloxacin group preoperatively, on the day of surgery, and postoperatively. There were no reports of adverse drug reactions for the 801 eyes in this surveillance. There were no differences between the besifloxacin and moxifloxacin treatment groups in rates of unexpected corneal findings (2.1% vs 1.5%, $P = 0.949$). The distribution of final visual acuity for the besifloxacin and moxifloxacin groups were similar ($P = 0.793$). Most cases had a final visual acuity of 20/20 or better.

Conclusion: In this retrospective surveillance study, the prophylactic use of besifloxacin ophthalmic suspension 0.6% and moxifloxacin ophthalmic solution 0.5% in patients undergoing LASIK surgery was not associated with any adverse drug reactions.

Keywords: Besivance, refractive surgery, adverse drug reactions LASIK, moxifloxacin ophthalmic solution 0.5%, ocular infection prophylaxis

Introduction

Laser-assisted in situ keratomileusis (LASIK) is a common keratorefractive procedure used for patients with myopia, hyperopia, and astigmatism, with an estimated 700,000 LASIK surgery procedures performed each year in USA alone.[1] In LASIK, the surgeon uses a microkeratome or femtosecond laser to create a flap of the corneal epithelium to access the corneal stroma. The flap of corneal epithelium is then elevated to create access to the underlying stromal tissue. Following excimer laser ablation of targeted stromal tissue to reshape the curvature of the corneal stroma, the flap is repositioned. This results in reduced pain and a quicker recovery in patients undergoing LASIK compared to those undergoing photorefractive keratectomy in which the central corneal epithelium is removed entirely.[2–4] LASIK surgery is generally preferred by patients[5] and is currently the most common keratorefractive procedure performed.[6–9]

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In LASIK, as with any keratorefractive procedure, a topical antibiotic or antiseptic may be applied preoperatively to the eye, and a topical nonsteroidal anti-inflammatory drug (NSAID) may also be applied to help ameliorate any postoperative pain.[9] Standard postoperative care includes the use of topical antibiotics to minimize the risk of postoperative infection, short term topical corticosteroids to reduce inflammation and minimize the risk for diffuse lamellar keratitis, and frequent lubrication with artificial tears.[9–11] The short-term use of a protective eye shield is also recommended.[9] Infection is uncommon following LASIK but has been reported following both initial procedures and retreatments.[7,12–17] Clinical signs and symptoms of infectious keratitis after LASIK generally include anterior chamber reaction, redness, pain, and photophobia.[9] Causative species appear to be staphylococci and atypical mycobacteria,[6,7,17–19] with the latest results of a survey conducted by the American Society of Cataract and Refractive Surgery[20] suggesting that the incidence of infectious keratitis due to methicillin-resistant *Staphylococcus aureus* (MRSA) is increasing while that due to atypical mycobacteria has decreased significantly. The decrease in mycobacterial keratitis following LASIK has been attributed to improved aseptic surgical techniques, such as the consistent use of povidone-iodine lid preps,[6,20] and the introduction of ophthalmic fourth generation fluoroquinolones, although the latter seems less likely based on reported in vitro minimum inhibitory concentrations of these drugs against mycobacterial isolates.[21] According to the American Academy of Ophthalmology preferred practice pattern on refractive surgery, there are currently no controlled investigations that establish optimal regimens of topically applied antibiotics, corticosteroids, NSAIDs and lubricating agents to use in postoperative care; therefore it is the decision of the operating surgeons as to what postoperative regimen to use.[9]

Besifloxacin ophthalmic suspension 0.6% (Besivance®, Bausch & Lomb, Inc., Rochester, NY) is a topical chlorofluoroquinolone formulation approved by the Food and Drug Administration in May 2009 for the treatment of bacterial conjunctivitis.[22–27] Besifloxacin has potent broad-spectrum bactericidal activity, including activity against multidrug-resistant staphylococcal isolates[28–31] and activity against mycobacterial species.[21] The in vitro potency of besifloxacin against MRSA has been reported to be better than that of either gatifloxacin or moxifloxacin and comparable to that of vancomycin.[28–32] Like other fluoroquinolones, it is being used in prophylactic antibiotic regimens by ocular surgeons. Besifloxacin ophthalmic suspension is formulated with DuraSite (InSite Vision, Alameda, CA), a polycarbophil-based mucoadhesive polymer designed to prolong a drug's residence time on the ocular surface and improve bioavailability.[33–36]

The aim of this retrospective surveillance study was to determine the safety profile of besifloxacin ophthalmic suspension 0.6% when used prophylactically in LASIK patients with a focus on types and rates of adverse drug reactions (ADRs). For comparison, retrospective data was also collected for moxifloxacin ophthalmic solution 0.5% (Vigamox® Alcon Laboratories, Inc, Fort Worth, TX).

Methods

Study design

This was a retrospective surveillance study of LASIK cases, where besifloxacin or moxifloxacin were prescribed as postoperative medication. Surgical centers were asked to provide data from consecutive cases dating back no longer than June 1, 2009. The study protocol was approved by Schulman Associates Institutional Review Board, Inc (Cincinnati, Ohio). An informed consent waiver was obtained as participating surgical centers provided data from retrospective cases in a manner that the subject could not be identified.

Refractive surgeons or their personnel were asked to provide retrospective case information on surgical outcomes. For each consecutive LASIK case in which besifloxacin ophthalmic suspension 0.6% or moxifloxacin ophthalmic solution 0.5% was prescribed as a perioperative medication, participating clinical investigators and their study personnel were asked to complete an Electronic Data Collection (EDC) form. The investigator was required to verify that all of the requested information was accurately recorded on the EDC form. For each site, the EDC form was numbered sequentially for each case, and a block of numbers was provided to each site.

Data to be collected on the EDC form included demographics (date of birth, gender), relevant comorbid conditions (diabetes, glaucoma, history of smoking, or other), surgical details (date of surgery, surgical eye, flap technique, preoperative corneal thickness, flap thickness, magnitude of correction, ablation depth, and whether or not there were intraoperative complications), medications used pre-, intra-, and postoperatively (daily dose, start date, end date for preoperative and postoperative medications; instillation regimen on day of surgery), and surgical outcomes. Information collected on surgical outcomes included any unexpected corneal findings (including abnormal postoperative endothelial morphology, abnormal edema, abnormal flap/wound healing

integrity, or corneal infiltrates) and final visual acuity (VA). Any adverse events considered related to the antibacterial, ie, ADRs, were recorded; or if none occurred, the absence of ADRs was recorded. Information to be collected for each ADR included onset date, stop date, eye (left eye [OD] or right eye [OS]), severity (mild, moderate, or severe), action taken with treatment (drug withdrawn, dose reduced, dose increased, dose unchanged, or unknown), relationship to antibacterial (possibly, probably, or definitely), action (no action, medicine, non-drug therapy, or surgery), outcome (resolved, resolved with sequelae, resolving, fatal, not recovered, or unknown), and whether or not the ADR was serious.

Analysis

The primary endpoint was the incidence of ADRs. A sample size of 500 besifloxacin cases was estimated to provide 95% confidence in detecting ADRs at a frequency of at least 0.6%.

All summaries were done at the eye level with two eyes from the same subject treated as two separate records. Continuous data were summarized using descriptive statistics (number, mean, standard deviation, median, minimum, and maximum) presented by treatment group. Summaries for discrete variables included the tabulation of frequencies and percentages by treatment group.

Surgical outcomes were compared using the Cochran-Mantel-Haenszel test controlling for study site or using Fisher's exact test without controlling for site. All statistical tests were carried out using a two-sided α level of 0.05. All statistical analyses were performed using SAS version 9.1.3 (SAS Institute Inc., Cary, NC, USA).

Results

A total of 801 case reports (801 eyes of 444 patients; n = 534 for besifloxacin, n = 267 for moxifloxacin) were obtained from nine private surgical centers. Three centers provided besifloxacin cases only (n = 311), two centers provided moxifloxacin cases only (n = 103), and the remaining centers provided both besifloxacin and moxifloxacin cases (n = 223 and n = 164). All refractive procedures were performed between August 2011 and December 2011. Table 1 presents the baseline characteristics of the study population. Mean (SD) age at the time of surgery was 36.1 (10.6) years, and most (57.6%) patients were female. Patients were generally healthy, with few comorbid conditions at the time of surgery.

Table 2 presents the frequency and duration of topical antibacterial use. Preoperatively, besifloxacin was used in more cases than was moxifloxacin (46.3% [247/534] vs 37.8% [101/267]), but when used, the frequency of preoperative besifloxacin dosing was lower than that of moxifloxacin. All cases received antibacterial drops on the day of surgery. However, as was the case preoperatively, the number of drops on the day of surgery was lower in besifloxacin cases compared to moxifloxacin cases, with a mean (SD) of 2.4 (1.2) drops for besifloxacin cases and 4.6

Table 1 Baseline characteristics (801 eyes of 444 patients)

	Besifloxacin ophthalmic suspension 0.6% (n = 534)	Moxifloxacin ophthalmic solution 0.5% (n = 267)	Total (n = 801)
Age at time of surgery (y)			
Mean (SD)	36.1 (10.5)	36.0 (10.6)	36.1 (10.6)
Median (range)	35 (18–78)	34 (18–74)	34 (18–78)
Gender, n (%)			
Male	229 (42.9)	111 (41.6)	340 (42.4)
Female	305 (57.1)	156 (58.4)	461 (57.6)
Comorbid conditions, n (%)			
Diabetes	6 (1.1)	6 (2.2)	12 (1.5)
Glaucoma	4 (0.7)	0	4 (0.5)
Smoker	25 (4.7)	8 (3.0)	33 (4.1)
Other	10 (1.9)	18 (6.7)	28 (3.5)

Abbreviation: SD, standard deviation.

Table 2 Frequency and duration of antibacterial used

	Besifloxacin ophthalmic suspension 0.6% (n = 534)	Moxifloxacin ophthalmic solution 0.5% (n = 267)
Preoperative use		
Eyes, n (%)	247 (46.3)	101 (37.8)
Frequency, n (%)[a]		
1 time daily	0	0
2 times daily	61 (24.7)	0
3 times daily	181 (73.3)	0
4 times daily	5 (2.0)	100 (99.0)
>4 times daily	0	1 (1.0)
Total drops on day of surgery		
Mean (SD)	2.4 (1.2)	4.6 (2.0)
Median (range)	2 (1–9)	5 (1–7)
Postoperative use		
Eyes, n (%)	534 (100)	267 (100)
Frequency, n (%)[a]		
1 time daily	0	0
2 times daily	60 (11.2)	0
3 times daily	268 (50.2)	1 (0.4)
4 times daily	206 (38.6)	263 (98.5)
>4 times daily	0	3 (1.1)
Duration, days[b]		
Mean (SD)	8.6 (2.2)	8.0 (2.3)
Median (range)	8 (4–30)	7 (2–15)

Notes: [a]Based on eyes treated. [b]Duration of antibacterial use is the sum of preoperative and postoperative antibacterial use.
Abbreviation: SD, standard deviation.

(2.0) drops for moxifloxacin cases. Of note, 31.8% (170/534) of besifloxacin cases and 97.0% (259/267) of moxifloxacin cases had drops applied directly to the flap interface. All cases received antibacterial drops postoperatively. The postoperative dosing frequency was lower in besifloxacin cases compared to moxifloxacin cases; postoperatively, 50.2% (268/534) of besifloxacin cases were on a three times daily (TID) regimen while 38.6% (206/534) were on a four times daily (QID) regimen. In contrast, 98.5% (263/267) of moxifloxacin cases were on a QID regimen postoperatively. Overall, the mean (SD) duration of antibiotic treatment was comparable in the treatment groups: 8.6 (2.2) days in the besifloxacin treatment group compared with 8.0 (2.3) days in the moxifloxacin treatment group.

As expected in patients undergoing refractive surgery, concurrent treatments included topical corticosteroids, NSAIDs, and artificial tears. Overall, 97.3% (779/801) of eyes were treated with corticosteroids, 13.6% (109/801) were treated with NSAIDs, and 99.5% (797/801) were treated with artificial tears (Table 3). The most frequently used corticosteroids were loteprednol etabonate 0.5% (Lotemax, Baush and Lomb Incorporated) and prednisolone acetate 1% (Pred Forte, [Allergan, Irvine CA]/Omnipred, [Alcon Laboratories, Inc, Fort Worth, TX]), while the most frequently used NSAID was ketorolac tromethamine (Acuvail). Most cases used a preservative-free artificial tear.

In both treatment groups, corticosteroids were most often used QID. The mean (SD) duration of treatment with corticosteroids was 13.1 (9.3) days in the besifloxacin treatment group and 7.7 (3.2) days in the moxifloxacin treatment group. NSAIDs, used in few cases overall, were used in fewer besifloxacin than moxifloxacin cases (5.6% vs 29.6%) and, when used, were used at a lower frequency in besifloxacin cases compared to moxifloxacin cases. For those cases that received NSAIDs, the most common dose regimen was QD in the besifloxacin treatment group with a mean (SD) duration of 15.5 (7.3) days compared to QID in the moxifloxacin treatment group for 4.4 (6.5) days. For both besifloxacin and moxifloxacin cases that received artificial tears, the most common dose regimen was more than four times daily. The mean (SD) duration of treatment with artificial tears was 79.4 (86.2) days in the besifloxacin treatment group and 84.2 (102.3) days in the moxifloxacin treatment group.

Surgical details are presented in Table 4. Flaps for most cases were created by laser. Within the besifloxacin treatment group, 63.5% of flaps were created with a laser and 36.5% were created with a microkeratome. Within the moxifloxacin treatment group, 74.9% were laser cases and 25.1% were microkeratome cases. Preoperative corneal thickness, flap thickness, ablation depth, and correction magnitudes were comparable in the treatment groups.

Table 3 Frequency and duration of corticosteroid, NSAID, and artificial tear use

	Besifloxacin ophthalmic suspension 0.6% (n = 534)	Moxifloxacin ophthalmic solution 0.5% (n = 267)
Corticosteroid use		
Eyes, n (%)	512 (95.9)	267 (100)
Frequency, n (%)[a]		
3 times daily	9 (1.8)	2 (0.7)
4 times daily	378 (73.8)	263 (98.5)
>4 times daily	125 (24.4)	2 (0.7)
Duration, days		
Mean (SD)	13.1 (9.3)	7.7 (3.2)
Median (range)	8 (6–56)	8 (1–40)
NSAID use		
Eyes, n (%)	30 (5.6)	79 (29.6)
Frequency, n (%)[a]		
1 time daily	21 (70.0)	0
2 times daily	7 (23.3)	21 (26.6)
3 times daily	0	8 (10.1)
4 times daily	2 (6.7)	50 (63.3)
Duration, days		
Mean (SD)	15.5 (7.3)	4.4 (6.5)
Median (range)	17 (2–36)	2 (2–48)
Artificial tear use		
Eyes, n (%)	530 (99.3)	267 (100)
Frequency, n (%)[a]		
1 time daily	35 (6.6)	0
2 times daily	2 (0.4)	0
3 times daily	0	0
4 times daily	121 (22.8)	105 (39.3)
>4 times daily	372 (70.2)	162 (60.7)
Duration, days		
Mean (SD)	79.4 (86.2)	84.2 (102.3)
Median (range)	43 (1–703)	43 (1–509)

Note: [a]Based on eyes treated.
Abbreviations: NSAID, nonsteroidal anti-inflammatory drug; SD, standard deviation.

The primary endpoint was the incidence of ADRs defined as adverse events related to the antibacterial. There were no reports of ADRs in either the besifloxacin or moxifloxacin treatment groups.

Surgical outcomes are presented in Table 5. The proportion of eyes with an unexpected corneal finding was similar between treatment groups (2.1% [11/534] vs 1.5% [4/267] in the besifloxacin and moxifloxacin treatment groups, respectively; $P = 0.949$). No abnormal postoperative endothelial morphology was reported in either group. One case of abnormal corneal edema was reported for the besifloxacin treatment group and two cases were reported for the moxifloxacin treatment group. Seven cases of abnormal wound healing/

Table 4 Summary of surgical details

	Besifloxacin ophthalmic suspension 0.6% (n = 534)	Moxifloxacin ophthalmic solution 0.5% (n = 267)
Flap technique, n (%)		
Microkeratome	195 (36.5)	67 (25.1)
Laser	339 (63.5)	200 (74.9)
Pre-op corneal thickness (µm)		
Mean (SD)	553.1 (34.0)	568.5 (32.1)
Median (range)	550 (442–664)	570 (484–658)
Flap thickness (µm)		
Mean (SD)	114.4 (18.3)	110.9 (13.9)
Median (range)	110 (50–166)	110 (50–171)
Ablation depth (µm)		
Mean (SD)	59.6 (28.0)	63.0 (30.0)
Median (range)	56 (4–149)	59 (14–146)
Magnitude of correction		
Sphere (D)		
Mean (SD)	–2.2 (3.5)	–3.1 (2.6)
Median (range)	–3 (–9 to 8)	–3 (–9 to 9)
Cylinder (D)		
Mean (SD)	–0.2 (0.9)	–0.3 (0.9)
Median (range)	0 (–3 to 4)	0 (–4 to 3)
Axis[a]		
With the rule (±20°)	190 (46.1)	110 (47.2)
Against the rule (±20°)	110 (26.7)	56 (24.0)
Oblique	112 (27.2)	67 (28.8)

Note: [a]Cases with cylinder (n = 645).
Abbreviation: SD, standard deviation; D, diopters.

integrity were reported at one site where only besifloxacin was used. All cases that had etiologies unrelated to the antibacterial, were observed after the antibacterial treatment had ended, or resolved without altering antibacterial use. None affected the vision outcomes. Three cases of corneal infiltrates were reported for the besifloxacin treatment group and two cases were reported for the moxifloxcin treatment group. The distribution of final VA was similar in the besifloxacin and moxifloxacin groups ($P = 0.793$). As Figure 1 shows, final visual acuity was 20/20 or better in 74.0% of besifloxacin cases and in 71.2% of moxifloxacin cases.

Discussion

LASIK is currently the most common popular keratorefractive procedure used for correction of ametropia, due to quicker recovery and reduced pain.[1–9] As with any ocular surgery, LASIK surgery is associated with a small risk of ocular infection. While estimates to date vary, an incidence of 0.035% was reported by both a survey on post-LASIK infectious keratitis by the American Society of Cataract and Refractive Surgery and the largest study to date on the incidence of post-LASIK infectious keratitis.[18,37] Although the incidence is low, post-LASIK infectious keratitis is potentially devastating;[6,20,38] thus, prophylaxis with perioperative antibiotics is considered the current standard of care.[9] Besifloxacin ophthalmic suspension 0.6% is a chlorofluoroquinolone formulation approved for the treatment of bacterial conjunctivitis, but also used in perioperative prophylactic antibiotic regimens by ocular surgeons. The objective of this retrospective chart review was to assess the safety of besifloxacin ophthalmic suspension 0.6% when used prophylactically by LASIK patients. As besifloxacin is a relatively new topical antibacterial on the market, we sought to gain a better understanding of the safety profile of this topical antibiotic when used for this off-label indication. Cases in which moxifloxacin ophthalmic solution 0.5% was used were included for comparison.

Results of more than 500 consecutive cases of LASIK surgery showed that the perioperative use of besifloxacin

Table 5 Summary of surgical outcomes

	Besifloxacin ophthalmic suspension 0.6% (n = 534)	Moxifloxacin ophthalmic solution 0.5% (n = 267)	*P*-value
Any unexpected corneal findings, n (%)	11 (2.1)	4 (1.5)	0.949[a]
Abnormal postoperative endothelial morphology, n (%)	0	0	–
Abnormal corneal edema, n (%)	1 (0.2)	2 (0.7)	0.720[a]
Abnormal wound healing/integrity, n (%)	7 (1.3)	0	0.102[b]
Corneal infiltrates, n (%)	3 (0.6)	2 (0.7)	0.965[a]
Final VA, n (%)			0.793[b]
20/60 or worse	14 (2.6)	7 (2.6)	
20/50	2 (0.4)	2 (0.7)	
20/40	4 (0.7)	4 (1.5)	
20/30	32 (6.0)	19 (7.1)	
20/25	87 (16.3)	45 (16.9)	
20/20 or better	395 (74.0)	190 (71.2)	

Notes: [a]Cochran-Mantel-Haenszel test controlling for site; [b]Fisher's exact test.
Abbreviations: VA, visual acuity.

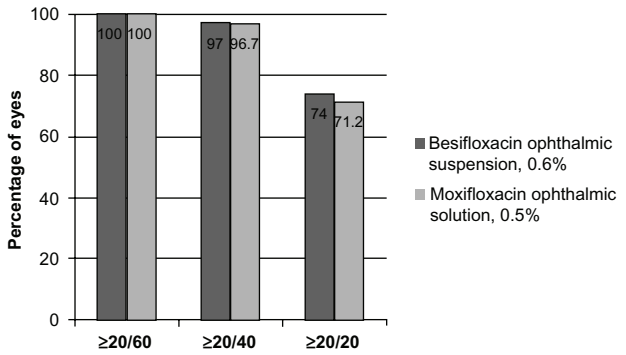

Figure 1 Final visual acuity.

ophthalmic suspension 0.6% did not result in any ADRs. Surgical outcomes were similar for the besifloxacin cases and moxifloxacin cases. Similar low rates of abnormal postoperative corneal findings were reported for the besifloxacin and moxifloxacin cases, with none attributed to the antibacterial medication used. Seven cases (1.3%) of abnormal wound healing were reported at one site where only besifloxacin ophthalmic suspension was used. The retrospective nature of this study limits the details of the cases to the chart recordings and prevents comparisons to other drugs because none was utilized at that site under the same conditions. Nevertheless, as indicated above, all seven cases had etiologies characterized as unrelated to the antibacterial used. In addition, Zhang et al[39] demonstrated a lack of effect of besifloxacin ophthalmic suspension on corneal reepithelialization in rabbits with full-thickness corneal epithelial defects. Perhaps more relevant, it has been suggested that carbomer-based lubricants (eg, Viscotears [Alcon], Celluvisc [Allergan]) may help prevent flap dislocation, due to their shear thinning properties.[40] Finally, in both treatment groups, a final VA of 20/20 or better was observed in >70% of cases, suggesting that visual rehabilitation was not affected by the choice of the topical antibiotic. This is an important finding, as LASIK surgery is an elective procedure with high patient expectations.

Perioperative regimens of topically applied antibiotics, corticosteroids, NSAIDs, and lubricating agents varied in this retrospective analysis of LASIK cases. This is likely due to the lack of controlled investigations that establish optimal regimens. The dosing frequency for besifloxacin was lower than that for moxifloxacin preoperatively, on the day of surgery, and postoperatively. While almost all patients were treated with corticosteroids, NSAID use was more common in the moxifloxacin treatment group than in the besifloxacin treatment group, and the dosing frequency was higher. Differences in NSAID use appeared to be related to differences in surgical practice rather than differences in treatment needs. At sites that included both besifloxacin and moxifloxacin cases, the NSAID-use profiles were similar. Two of the four sites contributing both besifloxacin and moxifloxacin cases reported a lower NSAID dosing frequency when using besifloxacin, while two sites reported QID NSAID dosing in both antibacterial treatment groups.

The results of this retrospective chart review are consistent with a previous retrospective chart review of routine cataract surgery cases where prophylactic besifloxacin or moxifloxacin was prescribed,[41] as well a recent prospective, parallel-group, investigator-masked study of besifloxacin ophthalmic suspension 0.6% and moxifloxacin ophthalmic solution 0.5% in cataract patients.[42] Parekh et al[41] evaluated the safety of besifloxacin ophthalmic suspension in the cataract surgery setting through a retrospective chart review of routine cases (phacoemulsification with posterior chamber intraocular lens implantation), where besifloxacin ophthalmic suspension 0.6% or moxifloxacin ophthalmic solution 0.5% was prescribed. As in our study, surgeons provided retrospective case information on surgical outcomes from consecutive cases and logged any adverse events related to the antibacterial used. Results of more than 700 consecutive cases showed that the perioperative use of besifloxacin did not result in any ADRs. Indeed, there were no reports of ADRs in either treatment group, and surgical outcomes were similar, as was the case in our analysis. Consistent with our study, daily dosing frequency was higher in the moxifloxacin group compared to the besifloxacin group ($P < 0.0001$).[41] Malhotra et al[42] studied corneal integrity in the eyes of 60 patients undergoing cataract extraction with intraocular lens (IOL) implantation. Patients received either besifloxacin ophthalmic suspension 0.6% or moxifloxacin ophthalmic solution 0.5% perioperatively in this prospective, investigator-masked study. All patients were assessed at baseline, at day 7, and at day 28 postoperatively. No adverse events were reported in either treatment group, and there were no differences between the two treatment groups in corneal endothelial cell density, corneal thickness, corneal staining, or intraocular pressure at any follow-up visit.

As described earlier, besifloxacin ophthalmic suspension is formulated with DuraSite (InSite Vision, Alameda, CA), a mucoadhesive polymer. The safety of the DuraSite vehicle itself was studied in animal models of ocular surgery by Krenzer and colleagues.[40] Krenzer et al studied the effect of topical administration of the DuraSite vehicle on surgically compromised rabbit eyes including eyes with a 3.0 mm clear corneal incision and eyes with a LASIK flap.[40] Eyes were

dosed with one drop of DuraSite (50 μL) QID for 1 day prior to surgery; 0.25 hours prior to surgery; 0.125, 4, and 8 hours after surgery; and then QID for an additional 9 days. No adverse effects were reported in either model of ocular surgery. In the corneal incision model, the polymer was not seen in the wound or the anterior chamber at any time, and assessment of the corneal endothelium showed normal healthy endothelium, which did not differ from the control. There were no adverse findings in the LASIK model that were considered related to DuraSite, and no polymer was observed at the interface. The histopathological results suggested that use of the DuraSite vehicle in these settings presented no unique safety concerns.

In conclusion, in this retrospective chart review, the prophylactic use of besifloxacin ophthalmic suspension 0.6% in patients undergoing LASIK surgery was not associated with any ADRs. In addition, surgical outcomes were similar to those obtained with moxifloxacin ophthalmic solution 0.5%. While the results of this study are consistent with those of previous studies evaluating the safety of besifloxacin ophthalmic suspension 0.6% in the perioperative setting, further prospective studies in LASIK patients are needed to confirm these findings.

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