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Topical Antibiotic Prophylaxis on the Incidence of Edophthalmitis Following Phacoemulsification Sugery: A Comparison of Gatifloxacin Versus Polymyxin B-Trimethoprim

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Abstract

***Purpose:** To compare two different perioperative topical antibiotic regimens on the incidence of endophthalmitis following phacoemulsification surgery.*

***Setting:** Lahey Hospital & Medical Center, Peabody, Massachusetts.*

***Design:** Retrospective, consecutive, observational case series.*

***Methods:** The electronic medical records were reviewed for 21,620 consecutive eyes of 13,529 patients undergoing phacoemulsification surgery during an eleven year period from June 2004 to June 2015. All eyes received topical ophthalmic antibiotic drops one hour before surgery. 13,859 consecutive eyes received topical gatifloxacin 0.3% ophthalmic solution and 7,761 consecutive eyes received topical polymyxin B sulfate 10,000 units-trimethoprim 1 mg/ml (PXTM) ophthalmic solution. Pearson chi-squared analyses were performed to examine differences between the two groups.*

***Results:** Over the study period, 5 cases of endophthalmitis occurred among 21,620 (0.023%) eyes following phacoemulsification surgery. The endophthalmitis rate did not differ between patients receiving topical gatifloxacin 0.3% compared to those receiving topical PXTM (0.0216% vs. 0.0258%, N.S.). Three cases of endophthalmitis occurred in 13,859 eyes receiving topical gatifloxacin 0.3% and 2 cases occurred in 7,761 eyes receiving topical PXTM (χ^2=0.037, p=0.85). Four cases were Gram positive species and one case yielded no growth. The switch in antibiotic prophylaxis resulted in no adverse events and led to an immediate cost-savings of nearly $80 per case.*

***Conclusion:** Endophthalmitis is rare following phacoemulsification surgery utilizing topical antimicrobial prophylaxis and without additional intracameral prophylaxis. The lack of difference in the rate of endophthalmitis following the switch from topical gatifloxacin 0.3% to PXTM supports the use of the latter, as it is a more cost effective agent.*

Prevention of surgical site infections (SSIs) continues to be a major focus in all surgical specialties. Endophthalmitis is an uncommon but potentially devastating complication of cataract surgery, with the primary source of infection being the patient's own flora.[1]

Reported rates of postoperative endophthalmitis from cataract surgery range from 0.04%-0.29%.[2-6] In order to decrease the risk of endophthalmitis, prophylactic measures are taken. The use of Povidone-iodine has been shown to be one of the most effective prophylactic treatments in the prevention of post-cataract endophthalmitis.[7,8] In addition, topical antibiotics are used perioperatively for prophylaxis against infection.[9,10] Topical fluoroquinolones have been widely used as prophylaxis in cataract surgery, with the fourth generation fluoroquinolones showing a significantly decreased incidence of endophthalmitis compared to prior generations.[11] Several studies have also shown a decreased incidence of endophthalmitis with the use of prophylactic intracameral antibiotics for phacoemulsification.[12-15]

However, in the era of developing antibiotic resistance, there is growing concern of overutilization of newer broad-spectrum antibiotics, especially for prophylaxis.[16,17] With the use of intracameral antibiotics, there are potential issues with sterility, errors in dilution, or the inadvertent use of preserved formulations leading to Toxic Anterior Segment Syndrome (TASS). Additionally, many of these newer antibiotics are costly, and it is important to evaluate whether the higher costs associated with these antibiotics contribute to quality of care.

In this study, we evaluated the use of the less costly topical antibiotic polymyxin B sulfate 10,000 units-trimethoprim 1 mg/ml (PXTM) ophthalmic drops (Sandoz, Inc., Princeton, NJ) to proprietary gatifloxacin [ophthalmic solution 0.3% (Zymar® Allergan, Inc., Licensed from Kyorin Pharmaceuticals Co., Ltd., Irvine, CA), a costlier antibiotic with no generic equivalent at the time of the switch to the former. Our study compared the incidence of endophthalmitis using perioperative topical gatifloxacin 0.3% ophthalmic solution versus topical PXTM ophthalmic solution.

Methods

Study Design: The study protocol was approved by the institutional review board of the Lahey Hospital and Medical Center (LHMC). The charts of all patients undergoing phacoemulsification in our hospital ambulatory surgery center were reviewed from June 2004 to June 2015. A total of 21,620 phacoemulsification surgery cases of 13,529 patients were reviewed: 13,859 consecutive eyes using perioperative gatifloxacin 0.3% ophthalmic drops from June 2004 to March 2012 and 7,761 consecutive eyes using perioperative PXTM ophthalmic drops from April 2012 to June 2015. One hour before surgery, all surgical eyes received either topical gatifloxacin 0.3% (Group I) or PXTM (Group 2) every 15 minutes for a total of 3 doses. All eyes received 5% povidone-iodine (Betadine® Purdue Pharma L.P., Stamford, CT) drops prior to surgery. No intracameral antibiotics were used.

Phacoemulsification surgeries were performed in two designated ophthalmic surgical operating rooms by 8 surgeons using a similar technique of small, corneal-limbal incision, phacoemulsification with intraocular lens (IOL) implantation.

No cases using gatifloxacin or PXTM were systematically excluded, regardless of intraoperative complications, e.g. ruptured posterior capsule, sulcus or anterior chamber intraocular lens implantation, corneal wound suture placement. Forty-four cases were excluded due to a substitution of an antibiotic other than topical gatifloxacin 0.3% or PXTM in 2012, as a result of drug shortage of gatifloxacin 0.3% occurring prior to the institutional switch to PXTM.

The postoperative topical antibiotic regimen was also switched in 2012 from topical gatifloxacin 0.3% ophthalmic solution to topical ofloxacin 0.3% ophthalmic solution (Ocuflox® Allergan, Inc. Irvine, CA) with frequency and duration based on surgeon preference due to both the expected cost savings to the patient and broader spectrum antibiotic coverage with the combination of PXTM and ofloxacin 0.3%. The savings associated with the switch to post-operative ofloxacin 0.3% is not included in the cost calculations because data specific to each case is not available.

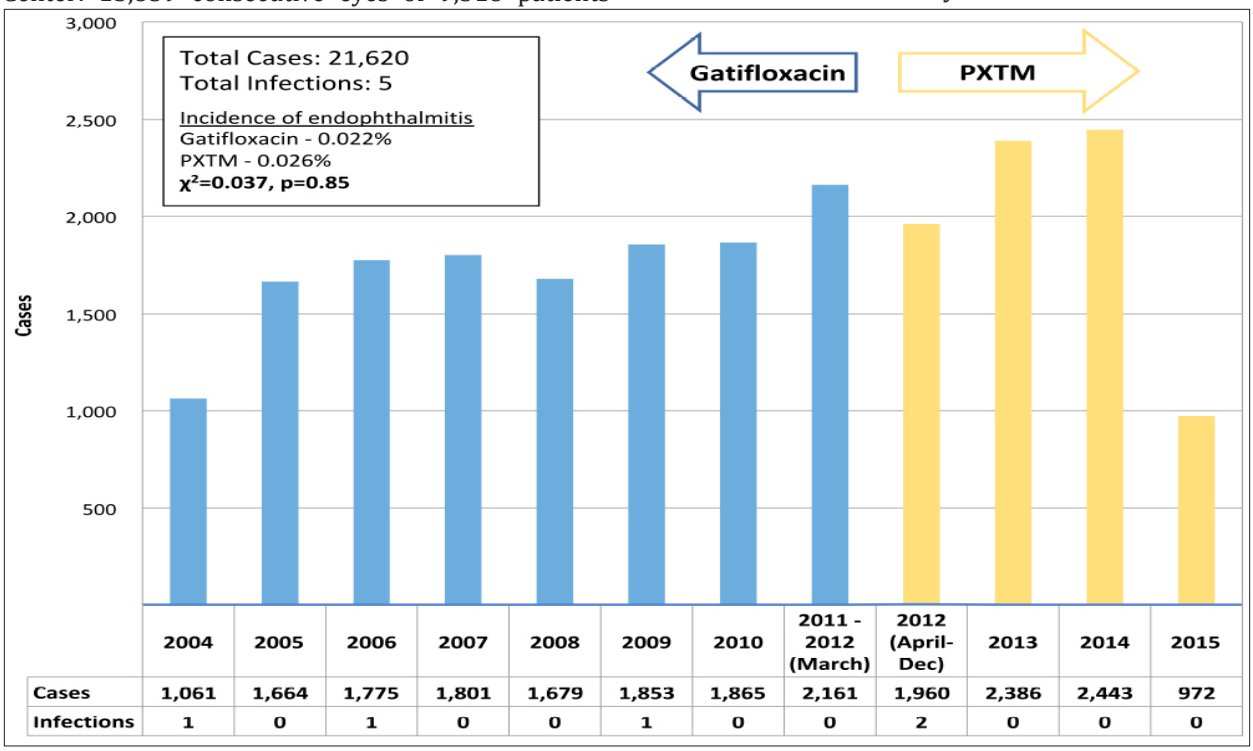
Statistical Analysis

To test whether there was a difference in the rate of endophthalmitis between the two groups following the change in perioperative antibiotic regimen, the Chi-squared statistic was calculated with SPSS® Statistics (version 22.0, IBM Inc., Armonk, NY). For these

analyses, it was not appropriate to adjust for surgeon- or patient-level factors because of the size of the study population and low incidence of endophthalmitis.

Results

21,620 eyes of 13,529 patients who underwent phacoemulsification surgery at the ambulatory surgery center of the Lahey Hospital and Medical Center: 13,859 consecutive eyes of 9,318 patients using perioperative topical gatifloxacin 0.3% followed by 7,761 consecutive eyesof 4,977 patients using topical PXTM. There were 766 patients who had one eye in the gatifloxacin group and the contralateral eye in the PTXM group. The average age of the patients was 74 years old in both groups. No adverse reactions, e.g. allergic reactions, were reported to either antibiotic over the course of the study.



	2004	2005	2006	2007	2008	2009	2010	2011 - 2012 (March)	2012 (April-Dec)	2013	2014	2015
Cases	1,061	1,664	1,775	1,801	1,679	1,853	1,865	2,161	1,960	2,386	2,443	972
Infections	1	0	1	0	0	1	0	0	2	0	0	0

Figure 1. *Number of phacoemulsification cases per year and corresponding number of infections from June 2004-June 2015. Pearson chi-squared analyses (insert) indicates no difference in the rate of endophthalmitis with gatifloxacin 0.3% (blue) vs. PTXM (yellow).*

The incidence of endophthalmitis was low regardless of the topical antibiotic used and not statistically significant: 3 cases in the gatifloxacin group at a rate of 0.22 per 1000(95% CI -0.0028% to 0.0461%) vs. 2 cases in the PXTM group at a rate of 0.26 per 1000 (95% CI -0.0099% ± 0.0615%), with χ^2=0.037, p=0.85 (Figure 1). Two of the five cases of endophthalmitis were complicated, with rupture of the posterior capsule requiring anterior vitrectomy. Both of these cases were in the gatifloxacin group. All five cases of endophthalmitis completed their full treatment course at the Lahey Hospital and Medical Center (LHMC). None of these five cases were lost to follow up during the first postoperative year. Three of the endophthalmitis cases occurred in the first eye: two of these patients had subsequent phacoemulsification surgery in the contralateral eye without incident, while one of the patients did not have contralateral eye surgery performed. Of the four endophthalmitis patients who had eye surgeries performed in both eyes, each eye was in the same group and there was no cross over in which one eye was in the gatifloxacin group and the other in the PXTM group. Each of the 5 cases identified in this case series was performed by a different surgeon. Four of the five cases grew out an organism, and in each of these cases a Gram-positive organism was identified: two coagulase negative *Staphylococcus spp.*, one case of a methicillin-resistant *Staphylococcus aureus* (MRSA), one case of a *Bacillus sp.*, and in one case the organism remained unidentified. Visual acuity at six months post treatment ranged from 20/20 to 20/50 (Table 1).

Table 1. *Endophthalmitis Cases*

Case#	1	2	3	4	5
Surgeon	A	B	C	D	E
Age	73	82	83	77	82
Sex	F	F	M	F	F
phaco date	September 2004	February 2006	August 2009	April 2012	August 2012
eye	OD	OS	OS	OS	OS
anesthesia	Topical	Peribulbar block	Peribulbar block	Topical	Topical
Incision	Temporal cornea	Temporal cornea	Temporal cornea	Temporal cornea	Temporal cornea
Suture	1 suture	1 suture	3 sutures	None	None
Lens Implant	Sulcus PCIOL	PCIOL	sulcus PCIOL	TORIC PCIOL	PCIOL
Intraoperative complications	Anterior vitrectomy	None	Anterior vitrectomy	None	None
Perioerative antibiotic drops	Gatifloxacin 0.3%	Gatifloxacin 0.3%	Gatifloxacin 0.3%	PTXM	PTXM
Intra-operative antibiotic supplement	None	None	Sub-conjunctival injection: cephalexin/ dexamethasone	None	None
Postop Antibiotic gtts	Gatifloxacin 0.3%	Gatifloxacin 0.3%	Gatifloxacin 0.3%	Ofloxacin 0.3%	Ofloxacin 0.3%
preop Va	20/60	20/200	20/200	20/60	20/40
Va POD #1	20/50	20/100	20/200	20/40	20/25
Endophthalmitis onset (days)	3	8	19	2	6
Presenting postop Va	CF	CF	HM	HM	CF
Presenting Symptoms	Decreased vision pain, redness	Decreased vision pain, redness	Decreased vision pain, redness	Decreased vision pain, redness	Decreased vision pain, redness
Presenting Signs	Hypopion	Hypopion	Hypopion	Hypopion	Hypopion
Treatment *	PPV/ intravitreal injection	AC tap/ intravitreal injection	AC tap/ intravitreal injection	AC tap/ intravitreal injection	AC tap/ intravitreal injection
Intravitreal antibiotic injection	Vancomycin amikacin	Vancomycin amikacin	Vancomycin ceftazadime	Vancomycin ceftazadime dexamethasone	Vancomycin ceftazadime
Aqueous results	n/a	Rare colonies of Methicillin-resistant *Staph. Aureus* (MRSA)	No growth	Rare Gram + rod Rare Gram + cocci pairs	n/a
Vitreous results	*Coagulase negative Staph*	n/a	n/a	n/a	*Coagulase negative cocci pairs*
Bacteria	Coagulase negative *Staphylococcus*	MRSA	no growth	*Bacillus sp.* (not *B. Anthracis*)	Coagulase negative *Staphylococcus*
Resistance	Ampicillin, penicillin, oxacillin augmentin cefazol	Erythromycin, levofloxacin, oxacillin, ciprofloxacin, cefazolin	n/a	Sensitivity testing for anaerobes not done by labs ordinarily	Erythromycin, oxacillin, tetracycline trimethoprim-sulfamethoxazole
Susceptible	Erythromycin, vancomycin, tetracycline trimethaprim-sulfamethoxazole	Trimethaprim-sulfamethoxazole, vancomycin, tetracycline, gentamycin	n/a	Sensitivity testing for anaerobes not routinely done by lab	Vancomycin, daptomycin, gentamicin, levofloxacin, linezolid, nitrofurantoin

Topical gtt sensitive potential	Not sensitive to fluoroquinolone	Sensitive to trimethoprim-sulfamethoxazole	n/a	Not sensitive to fluoroquinolone	Sensitive to fluoroquinolone
Postop antibiotic drops continued s/p IVA injection	Gatifloxacin 0.3%	Gatifloxacin 0.3%	Gatifloxacin 0.3%	Ofloxacin 0.3%	Ofloxacin 0.3%
VA s/p Intravitreal injection					
6 months	20/20	20/30	20/50	20/30	20/50**
* Treatment at date of presentation; no additional antibiotics aside from the intravitreal medications were used. ** Required 2nd PPV to clear visual axis at 1 month, no additional intravitreal antibiotics injected.					

Cost

At the time of the switch in 2012, the change from gatifloxacin to PXTM yielded a nearly $80 cost saving per case (Table 2). With the advent of generic gatifloxacin, the cost savings by the end of the study period declined to $60 per case, still a significant level of cost savings. Over the four year period, there was a cost savings for our institution of nearly $0.5M for our institution.

Coinciding with this change, the postoperative topical antibiotic regimen was also switched in 2012 from topical gatifloxacin 0.3% ophthalmic solution to topical ofloxacin 0.3% ophthalmic solution 0.3% (also available as a generic) frequency and duration based on surgeon preference. Based on Medicare copayment price, a further cost savings to the patient for a standard 5 mL bottle, equaling to nearly $64 per case might have been expected (Table 2), but the actual savings experienced by patients (or their insurance carrier) likely varied (data not available). The use of an eye drop available as a generic medication may also have accrued a benefit for certain patients for which these two medications were in different copayment or coinsurance tiers.

Table 2. *Antibiotic Eye Drop Cost*

Hospital cost ($/ml)*	Gatifloxacin 0.3%	PTXM
	$17.32	$0.75
Patient cost ($/ml)**	Gatifloxacin 0.3%	Ofloxacin 0.3%
	$16.60	$3.80
* LHMC Pharmacy average wholesale price (AWP) 2012 supply cost. ** Estimate based on average Medicare copay cost: Gatifloxacin 0.3% average Medicare copay cost - GoodRx. [Internet]. Santa Monica, CA: GoodRx, Inc., 2018. https://www.goodrx.com/zymar/medicare-coverage Ofloxacin 0.3% Medicare maximum copay cost- GoodRx. [Internet]. Santa Monica, CA: GoodRx, Inc., 2018. https://www.goodrx.com/oflocxacin/medicare-coverage		

Discussion

Endophthalmitis is usually caused by an infectious organism entering the eye at the time of intraocular surgery, particularly cataract surgery. Prevention of this uncommon but potentially devastating surgical complication remains a major focus for ophthalmic surgeons throughout all phases of surgical care. It is well known that SSIs result from a multitude of etiologies, and reducing the risk of SSI is not only associated with appropriate antibiotic prophylaxis but also associated with meticulous surgical site preparation and surgical technique. During the surgical procedure, factors that may influence SSI rates include wound construction, wound integrity, and complications in surgery such as ruptured posterior capsules.[1,18]

This study represents greater than a 10-year experience preventing SSIs following phacoemulsification surgery at the LHMC, an academic referral center. Our study of 21,620 cases over an eleven year period is comparable in length and sample size to many of the North American studies at a single institution reviewing rates of endophthalmitis with changes in management for phacoemulsification surgery.[9,11,14,15] The overall endophthalmitis rate in our eleven year study period (0.023%) compares

favorably with reported rates of endophthalmitis postoperatively from cataract surgery (0.04%-0.29%), including those utilizing intracameral antimicrobial prophylaxis.[2-6, 11-15] The endophthalmitis prevention studies conducted by Shorstein et al.[14] (consisting of a retrospective review of 16, 264 phacoemulsification surgeries with and without intracameral antibiotic use) and Jensen et al.[11] (consisting of a retrospective review of 29,276 phacoemulsification surgeries comparing postoperative use of topical third generation fluoroquinolones vs. fourth generation fluoroquinolones) both showed a significant decrease in endophthalmitis following their interventional changes. In contrast, following a standardized institutional protocol, our already low overall rate of endophthalmitis did not change.

To our knowledge, our study is the largest case series comparing perioperative topical antibiotic use in phacoemulsification surgery without intracameral antibiotic use at a single institution. Shorstein et al.[14] reported declining infection rates with the adoption of intracameral antibiotics, from 0.31% (9/2,878) to 0.075% (10/13,386 total intracameral antibiotic use). Our rate is lower than the total rate they report with intracameral antibiotics ($p=0.024$). In comparison with the ESCRS study, the endophthalmitis rate at the LHMC was significantly lower than the rate reported in patients receiving topical perioperative levofloxacin eye drops (0.292%, $p<0.001$), and statistically indistinguishable from the overall rate reported with intracameral agents (0.073%, $p=0.055$).[13] Similarly, our rate of endophthalmitis was lower than the rate reported in the large study of phacoemulsification and manual small-incision cataract surgery done by Haripriya et al. without intracameral moxifloxacin (0.071%, $p=0.009$) and comparable to the rate with intracameral moxifloxacin (0.020%, $p=0.78$).[15]

Approximately 48-70% of all endophthalmitis infections that occur postoperatively are caused by coagulase-negative *Staphylococcus*.[1,8,13,17] In order to prevent the likelihood of infection, prophylactic antibiotics are used against these organisms, although no class of antibiotic has an approved indication for topical perioperative use.[20] The change in our perioperative topical antibiotic from gatifloxacin 0.3% to PXTM occurred due to the significant cost of gatifloxacin and lack of evidence to warrant its continued use in this setting. The antibiotic PXTM was studied for perioperative use to evaluate if it provided an equal, but less expensive alternative to the standard gatifloxacin 0.3% ophthalmic drops. It was hypothesized that the less expensive PXTM would be as effective as gatifloxacin 0.3% in preventing bacterial endophthalmitis. We found no difference in the rate of endophthalmitis following the switch from gatifloxacin 0.3% to PXTM. Although the antibiotic spectrum between these two drugs differs slightly in their coverage of skin flora bacteria, this did not affect the rate of endophthalmitis, supporting the conclusion that PXTM is equally effective, yet had the added benefit of being less costly.

In our study, there was also a concurrent switch in the post-operative topical antibiotic regimen in 2012 from topical, non-generic gatifloxacin 0.3% ophthalmic solution to generic, topical ofloxacin 0.3% ophthalmic solution. This within-class switch was also made due to an expected cost savings to the patient. Although the switch from one fluoroquinolone postoperative eye drop regimen to another could have had an impact on SSIs, the role of postoperative drops in SSI prevention is even less certain.[11] Neither agent has an indication for topical perioperative use, and this study is not powered to examine the impact of patient-level factors. The additional coverage of Gram-negative organisms by ofloxacin may confer a theoretical benefit from the use of this agent over gatifloxacin for certain organisms, e.g. the additional activity against *Pseudomonas aeruginosa*. This is less likely important as most organisms identified in cases of endophthalmitis are Gram-positive organisms.[1,16,18,21] Furthermore, it is well known that patient compliance with eye drops is less than complete, making the impact of postoperative drops likely the least significant component of the preventative triad of perioperative, intraoperative, and postoperative measures against infection.

PXTM was selected as a substitute to gatifloxacin 0.3% because of its antibacterial coverage against *Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pneumoniae, Streptococcus viridans, Haemophilus influenzae* and *Pseudomonas aeruginosa*, many of which are most frequently known to cause endophthalmitis.[16,21] In addition, both trimethoprim and sulfamethoxazole have been shown to have activity against MRSA.[22] Although ofloxacin does

Table 3. *Outpatient Antibiotic Retail Cost*

Patient retail cost ($/ml)*	Gatifloxacin 0.3%	Ofloxacin 0.3%
	$43.96	$9.95
* Estimate based on average retail cost: Gatifloxacin price and gatifloxacin coupons - GoodRx. [Internet]. Santa Monica, CA: GoodRx, Inc., 2018. https://www.goodrx.com/gatifloxacin Ofloxacin price and ofloxacin coupons - GoodRx. [Internet]. Santa Monica, CA: GoodRx, Inc., 2018. https://www.goodrx.com/oflocxacin		

not have the Gram-positive coverage spectrum of gatifloxacin, our rationale for the postoperative topical antibiotic regimen change from gatifloxacin 0.3% to ofloxacin 0.3% was two-fold. First, ofloxacin has been shown to have intraocular penetration,[23] an important effect in the postoperative setting, and along with the Gram-positive effects of PXTM preoperatively, supported a broad range of antibacterial coverage. Second, the cost of ofloxacin 0.3% may be up to 4.5x less than gatifloxacin 0.3% (Table 2). This change in the perioperative and postoperative regimen was adopted in April of 2012 at the LHMC.

Although antibiotics are part of standard perioperative eye care to decrease the risk of infection, the topical application of povidone-iodine in cataract surgery is the most effective prophylaxis known to date in reducing infection than prophylactic antibiotic usage alone and has the same bactericidal effect as a three-day antibiotics course.[24] According to the pivotal study conducted in 1990 by Speaker et al. the perioperative use of povidone-iodine had a significant effect on infection rate reduction compared to the type of antibiotic used: patients treated with povidone-iodine and topical antibiotics for prophylaxis exhibited a statistically lower endophthalmitis infection rate compared to those who received only prophylactic antibiotics.[7] In our study, all cases received preoperative topical povidone-iodine 5% drops 15 minutes before surgery and 10% povidone-iodine for the periocular skin to prepare the surgical field prior to draping at the time of surgery, along with perioperative topical gatifloxacin 0.3% or PXTM one hour prior to surgery. Nentwich et al. showed a significant decline in endophthalmitis with a standardized protocol using topical antibiotics and copious irrigation of povidone-iodine.[8]

During the study period (2004 to 2015), there were a total of five endophthalmitis cases at LHMC. The *Staphyloccocus* genus caused three of the five cases of endophthalmitis: two were coagulase-negative *Staphylococcus species*and one was MRSA. The MRSA case occurred in Group 1 (gatifloxacin group) and was susceptible to trimethoprim B, but at the time of this infection gatifloxacin 0.3% was in use both peri- and postoperatively. None of these cases were sensitive to fluoroquinolone antibiotics. The coagulase negative *Staphylococcus sp.* in Group 1 was found to be sensitive to PXTM, but the coagulase negative *Staphylococcus sp.* in Group 2 (PXTM group) proved to be resistant to this drug combination.

One case grew out *Bacillus,* a genus of gram-positive, rod-shaped bacteria, and although ofloxacin 0.3% was used postoperatively, this did not prevent the occurrence of endophthalmitis.

Finally, in one case the organism remained unidentified. The unidentified organism caused both a hypopyon and vitritis, likely signifying a bacterial infection and resolved with intravitreal antibiotic treatment. No growth occurred in the culture of the aqueous fluid, in part due to the small sample size.[25] Although the unidentified organism produced signs and symptoms at a later onset (19 days) postoperatively than the other cases, this is within the timing of endophthalmitis with corneal incision cataract surgery.[26] Olson et al. reported 13 days as the mean time between cataract surgery and diagnosis of endophthalmitis (range, 1-39 days).[26]

In 2012, the pharmaceutical supply cost at LHMC for a 5mL bottle of Zymar™, the brand name for gatifloxacin was 23x the cost of a generic 5mL bottle of PTXM (Table 2). Based on finding no clear evidence that one antibiotic was superior to the other as a means of prophylaxis and in an effort to standardize practice and streamline costs, PXTM became the standard perioperative antibiotic for cataract surgery at LHMC in April 2012.

Over the study period, the change in choice of topical

antibiotic agent from gatifloxacin to PTMX is estimated to have saved our institution nearly $0.5M. However, a formal cost-effectiveness analysis may be required to capture full economic and health consequences of the switching behavior. Cost comparisons of commonly used postoperative topical ophthalmic antibiotics is expected to be of increasing importance as the number of cataract surgeries is expected to increase with the growing aging population.[5,27] Our current endophthalmitis rate with the perioperative use of topical antibiotics and without intracameral agents compares favorably with the European Society of Cataract and Refractive Surgeons (ESCRS) multicenter study which utilized intracameral antibiotics perioperatively.[13] Intracameral antibiotics add cost and certain agents have been associated with rare, but potentially devastating postoperative conditions, such as vancomycin-associated postoperative hemorrhagic occlusive retinal vasculitis and toxic anterior segment syndrome (TASS).[28,29]

Study Limitations

Because this study was conducted retrospectively, many factors within and outside of the perioperative environment may have influenced the infections, such as variability in technique between surgeons, the preoperative surgical preparation of the eye and ocular surface, as well as patient hygiene and compliance with postoperative regimen. A prospective, multi-center, randomized, double-blind, controlled study would provide stronger evidence to support the hypothesis that PTXM is non-inferior to gatifloxacin prophylaxis.

Our study, similar to previous studies on this topic, has limited statistical power to detect a difference between the groups.[30] Assuming the highest reported frequency of endophthalmitis of 0.34%,[13] the rate would need to more than double to have an 80% power to detect a difference with an α =0.05 with our current sample size. If the actual endophthalmitis rate is closer to the lower limit of 0.04%[3] (higher than the rate observed at the LHMC), a nationwide randomized controlled trial that included nearly all of the more than 3 million eyes[6] that undergo uncomplicated cataract extraction each year in the United States would have an 80% power to detect only an approximately 20% rise in the rate of endophthalmitis between equal size cohorts.

Conclusion

There are no specific guidelines for administration of prophylactic antibiotics for cataract surgery in the United States,[20] and the American Association of Ophthalmology states, "Specific prophylactic antibiotic strategies in the perioperative period lack sufficient scientific evidence to make recommendations at this time," (American Academy of Ophthalmology, 2016), and the Canadian Ophthalmological Society recommends that if the surgeon has a higher endophthalmitis rate than published norms, consideration should be given to change to intracameral or subconjunctival antibiotic supplementation (Canadian Ophthalmological Society Cataract Surgery Clinical Practice Guideline Expert Committee, 2008).

Changing the antibiotic regimen from gatifloxacin 0.3% ophthalmic drops to PXTM ophthalmic drops did not alter the observed rate of endophthalmitis in our patients undergoing cataract surgery. This change of regimen provided equivalent protection from infection, was without adverse events, and yielded a substantial cost savings for both patients and our institution. With the growing cost of medical care, particularly prescription drug costs, identifying settings where less costly antibiotics provide equally effective prophylaxis may result in substantial savings for the health system. Using expensive or newer drugs without evidence for proportional benefits is not warranted. With such low rates of endophthalmitis, such a switch in regimen may be reasonable even with the aforementioned uncertainties.

What Was Known

- Although the use of perioperative topical povidone-iodine has been shown to be the most effective method to prevent endophthalmitis, topical antibiotic prophylaxis is typically added to further decrease the risk on infection from eye surgery.
- A wide variety of perioperative topical antibiotic regimens are in use in the absence of any head-to-head comparisons in phacoemulsification surgery, apart from those studying the addition of intracameral antibiotics.
- There is growing concern over antibiotic resistance and overuse of newer and more expensive antibiotics, without evidence for proportional value to the patient or healthcare system.

What This Paper Adds

- The rate of endophthalmitis in phacoemulsification surgeryis extremely low regardless of a change in perioperative topical antibiotic regimen and without the use of intracameral antibiotics.
- System-wide adoption of a less costly, topical antibiotic perioperatively showed no change in infection rate and no adverse effects.
- The endophthalmitis rate reported at an academic referral center utilizing only topical antibiotics following a standardized institutional protocol was lower than the rates reported by the ESCRS studies using topical antibiotics alone, and indistinguishable to the rate reported with intracameral agents.

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