

# Efficacy of Prophylactic Intracameral Moxifloxacin in Cataract Surgery

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## ABSTRACT

**Purpose:** To determine the efficacy of prophylactic intracameral moxifloxacin 0.5% ophthalmic solution (Vigamox) in preventing postoperative endophthalmitis in patients having cataract surgery.

**Material and methods:** The study was conducted at Alkhair Lions Eye Hospital, Lahore, from February 2010 to April 2011. Preoperative and final 1-month postoperative anterior chamber reaction was assessed in 650 eyes that had cataract surgery with intracameral moxifloxacin. All eyes received 0.1 mL intracameral moxifloxacin 0.5% ophthalmic solution containing 500 mg of moxifloxacin as the last step of cataract surgery. Patients were followed up for one month. Patients with any major intraoperative complication or who were lost to follow-up were excluded.

**Results:** 615 eyes completed the study. The mean age was 69.5 years (range 48 to 84 years). All eyes had quiet anterior chamber preoperatively and had trace to +2 cells and flare anterior chamber reaction only on the first day after surgery. Postoperative evaluation was done on first day, after one week and finally after one month. There was no anterior chamber reaction and no endophthalmitis.

**Conclusion:** Intracameral moxifloxacin 0.5mg/mL appeared to be effective in preventing postop anterior chamber reaction and ultimately endophthalmitis in patients undergoing cataract extraction.

**Key words:** Prophylactic intracameral moxifloxacin, cataract,

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## INTRODUCTION

Postoperative endophthalmitis has always been a major threat and concern for the ophthalmologists all over the world. Postoperative anterior chamber reaction is an important predictor for this worst complication. Different methods have been adopted for the prevention of endophthalmitis. The use of prophylactic intracameral antibiotics is one of them. Among the antibiotics given intracamerally, most commonly used are cefuroxime and vancomycin<sup>1</sup>.

Before the introduction of moxifloxacin ophthalmic solution 0.5% (Vigamox), many surgeons used intracameral vancomycin at the conclusion of cataract surgery as part of the prophylactic regimen<sup>2</sup>. Although the risk for endophthalmitis was reduced with vancomycin, there was no strong proof that vancomycin prevents endophthalmitis<sup>3,4</sup>. In addition, one study conducted by Axer-Siegel et al showed that vancomycin increased the risk for clinically significant macular edema (CSME) as well as cystoids macular edema (CME) seen on fluorescein angiography 1 month and 4 months after cataract surgery<sup>5</sup>. Moreover, because of its potency, vancomycin has generally been reserved for treatment of infections that are not efficiently treatable by other drugs. Issues have been raised regarding the emergence of vancomycin-resistant

enterococci, an increase in intermediate resistance to vancomycin in coagulase-negative staphylococci, and methicillin-resistant *Staphylococcus aureus*. These issues and the lack of scientific proof of vancomycin's efficacy in preventing endophthalmitis led to a joint statement by the American Academy of Ophthalmology and the U.S. Centers for Disease Control discouraging the routine prophylactic use of vancomycin in ocular surgery<sup>6,7</sup>.

In contrast, in a preliminary report of the ESCRS Endophthalmitis Study Group, intracameral cefuroxime was shown to significantly reduce the risk for developing endophthalmitis after phacoemulsification cataract surgery<sup>8,9</sup>. However, like vancomycin, cefuroxime is available in a systemic preparation that must be reconstituted using saline solution before it can safely be delivered to the eye. Reconstituting the drug for intracameral use may increase the risk for toxic anterior segment syndrome (TASS) because an undesired concentration of the drug may be inadvertently injected if a mistake occurs during the preparation or dilution process. It is well known that incorrect drug concentration, incorrect pH, and incorrect osmolality can cause TASS<sup>10</sup>.

Considering the possible complications with vancomycin and cefuroxime, moxifloxacin seems to be the better choice of antibiotic for endophthalmitis prophylaxis because of its broad-spectrum coverage and mode of action.<sup>11</sup> Moxifloxacin is a fourth-generation fluoroquinolone antibacterial agent that is active against a broad spectrum of gram-positive and

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gram-negative ocular pathogens, atypical microorganisms, and anaerobes<sup>12-13</sup> (Tables 1 to 3). The ophthalmic solution is isotonic and formulated at pH 6.8 with an osmolality of approximately 290 mOsm/kg (product description, moxifloxacin hydrochloride ophthalmic solution 0.5%, Alcon Laboratories, reference: AAA083-0604); both values are within the compatible range for humans (pH 6.5 to 8.5 and osmolality 200 to 400 mOsm/kg). Vigamox is also a self-preserved (no added preservatives) commercial ophthalmic formulation that requires no special preparation for intracameral delivery, reducing the risk for TASS<sup>13</sup>. In addition, early studies of rabbit eyes did not show intraocular toxicity after injection of intravitreal or intracameral moxifloxacin<sup>12</sup>.

## PATIENTS AND METHODS

The study was conducted from February 2010 to April 2011 on patients of age 45 to 85 years with no ocular pathology other than cataract. Exclusion criteria included glaucoma, retinopathy, maculopathy, media opacity other than cataract (cornea or vitreous), and visual pathway problems. Patients with uveitis, diabetes, corneal endothelial disease, or pseudoexfoliation and those who were taking systemic immunosuppressants or anticoagulants were also excluded. Other exclusion criteria were intraoperative complications or difficulties and prolonged surgery and patients lost in follow up.

Pupils were dilated with a solution of tropicamide 1%. All surgeries were performed using peribulbar anesthesia of Bupivacaine and Lignocaine. Uneventful extracapsular cataract extraction with implantation of IOL was performed. At the end of surgery, intracameral moxifloxacin was given to each patient. The reason we went to intracameral antibiotic was that it just made sense to put the antibiotic at the site of potential infection.

Preoperatively, patients received 1 drop of topical Vigamox every 15 minutes at least 4 times. Povidone-iodine 0.5% was instilled into the cul de sac. At the start of the operating day, the contents of a newly opened bottle of Vigamox was aspirated into a sterile 10 cc syringe and set aside. With a tuberculin syringe, a volume slightly in excess of 0.1 mL (0.3 to 0.5 mL) of the pure moxifloxacin 0.5% ophthalmic solution was then aspirated from the 10 cc syringe. No solution, including saline, was added to dilute the commercial preparation. The excess amount was discarded, leaving 0.1 mL in the tuberculin syringe ready for injection into the anterior chamber. This volume contained 0.5 mg of the nonpreserved moxifloxacin with a pH of 6.8 and an osmolality of approximately 290mOsm/kg. The solution prepared in the syringe was injected using a

27-gauge cannula through the incision as the last step of cataract extraction and IOL implantation. Postoperative antibiotics included oral ciprofloxacin 500 mg, 1 tablet twice a day for 5 days. For First 48 hours, topical Tobramycin was given every 2 hourly. The Tobramycin was then reduced to 4 times a day for three weeks. Topical prednisolone acetate 1% (Pred Forte) was also given postoperatively using the same dosage schedule used for Tobramycin.

The patients were scheduled for follow-up at 1 day, 1 week, and 1 month after surgery. Anterior chamber reaction, expressed as cells and flare intensity, was graded by an independent observer using the Hogan system<sup>14</sup>. All observations were done using a slit lamp biomicroscope 1 day and 1 and 4 weeks after surgery.

## RESULTS

Out of 650 eyes, 615 eyes completed the study. All patients were Asian. The mean age of the 295 men and 320 women was 69.5 years (range 48 to 84 years). All eyes had trace to +2 cells and flare only on the first day after cataract surgery. On subsequent follow ups, anterior chamber was quiet in 99.18% (610 Patients). Only five patients had anterior chamber reaction on second follow up visit and were given topical steroids in higher frequency, which cured the uveitic reaction. No patient ended with endophthalmitis at the completion of study.

Table 1. Susceptibility of gram-positive species to moxifloxacin MIC50 (mg/mL)

Bacterial Species	Moxifloxacin
Staphylococcus aureus	0.03
Staphylococcus epidermidis	0.06
Staphylococcus haemolyticus	0.06
Staphylococcus saprophyticus	0.03, 0.13
Staphylococcus lugdunensis	0.13
Staphylococcus hominis	0.03, 0.06
Staphylococcus simulans	0.03
Staphylococcus pasteurii	0.06
Staphylococcus warneri	0.03, 0.06
Streptococcus pneumoniae	0.06, 0.13
Streptococcus mitis	0.13
Streptococcus viridans group	0.13
Streptococcus pyogenes	0.13, 0.25
Enterococcus faecalis	0.19, 0.25
Micrococcus luteus	0.50
Kocuria species	0.25
Bacillus cereus	0.09, 0.13
Bacillus pumilus	0.13
Bacillus subtilis	0.16
Corynebacterium accolens	0.03
Corynebacterium macginleyi	0.03
Corynebacterium propinquum	0.25
Corynebacterium pseudodiphtheriticum	0.25

MIC = minimum inhibitory concentration

Table 2. Susceptibility of gram-negative species to moxifloxacin MIC<sub>50</sub> (mg/mL)

Bacterial species	Moxifloxacin
Aeromonas caviae	0.13
Citrobacter koseri	0.03
Enterobacter aerogenes	0.06, 0.25
Enterobacter cloacae	0.03, 0.13
Enterobacter hormaechei	0.13
Escherichia coli	0.008, 0.06
Klebsiella oxytoca	0.03, 0.25
Klebsiella pneumoniae	0.03, 0.13
Morganella morgagnii	0.06, 0.50
Pantoea agglomerans	0.03, 0.06
Proteus mirabilis	0.06, 0.50
Serratia marcescens	0.25, 0.50
Achromobacter xylooxidans	2.0, 4.0
Acinetobacter baumannii	0.03, 0.13
Acinetobacter calcoaceticus	0.016, 0.06
Acinetobacter johnsonii	0.16, 0.13
Acinetobacter junii	0.06
Acinetobacter genospecies 3	0.016, 0.06
Chryseobacterium indologenes	0.25
Chryseomonas luteola	0.13
Stenotrophomonas maltophilia	0.13, 1.0
Pseudomonas aeruginosa	0.50, 2.0, 4.0
Pseudomonas oryzzihabitans	0.13
Pseudomonas stutzeri	0.25
Haemophilus influenza	0.016, 0.03, 0.39
Moraxella catarrhalis	0.03, 0.047, 0.06
Moraxella osloensis	0.13
Neisseria perflava	0.03

Table 3. Susceptibility of atypical and anaerobic species to moxifloxacin MIC<sub>50</sub> (mg/mL)

Bacterial Species	Moxifloxacin
<b>Atypical</b>	
Mycobacterium avium	3.2
Mycobacterium marinum	0.4
Mycobacterium chelonae	1.6, 8.0
Mycobacterium abscessus	8.0
Mycobacterium fortuitum	0.06
Mycobacterium kansasii	0.06
Chlamydia trachomatis	0.03
<b>Anaerobe</b>	
Propionibacterium acnes	0.25
Bacteroides fragilis	0.25
Clostridium perfringens	0.50
Peptostreptococcus species	0.25

To our knowledge, this is the first report of a topical ophthalmic preparation applied through the intraocular route as a prophylactic agent in cataract surgery.<sup>13</sup> Our study evaluated the efficacy of injecting intracameral Vigamox in human eyes having cataract surgery to prevent postoperative endophthalmitis.

## DISCUSSION

Endophthalmitis cases after cataract surgery increased from 1994 to 2001, with a reported incidence of 0.215%<sup>15</sup>. With only povidone iodine prophylaxis, incidence of endophthalmitis is 0.3-0.5% in Europe<sup>16, 17</sup> and 0.015% in USA. While in Pakistan this rate was found to be 0.6%<sup>18</sup>. The European Society of Cataract and Refractive Surgery (ESCRS) study has found the lowest observed incidence rates were for the group which received both intracameral and perioperative topical antibiotics<sup>9</sup>. Thus, there is a need for protective antibiotics to combat the rise and to better treat patients, especially in the light of increasing antibacterial resistance among causative organisms. Of the prophylaxis methods for cataract surgery, only povidone-iodine received intermediate clinical recommendation, as discussed by Ciulla et al<sup>19</sup> in a literature review of endophthalmitis prophylaxis. In addition, Isenberg et al.<sup>20</sup> found that povidone-iodine reduces conjunctival flora by 91% for colony-forming units and 51% for species when applied alone to the eye just before surgery; when applied in conjunction with a topical antibiotic, it produced a synergistic effect that led to sterilization of 83% of the eye. Although antiseptic agents such as povidone-iodine are effective for ocular surface decontamination, antibiotics with favorable pharmacodynamic properties are required to deliver ocular protection.

Fluoroquinolones were introduced for treatment of corneal and conjunctival infections; however, these antibiotics found a greater role in prophylaxis before surgery to prevent endophthalmitis. New generations of fluoroquinolones were introduced to counteract resistance to the second-generation agents. These include third-generation (levofloxacin) and fourth-generation (moxifloxacin and gatifloxacin) fluoroquinolones<sup>11</sup>.

Several studies<sup>11,13,21,22</sup> found moxifloxacin, a fourth-generation antibiotic, to be superior in terms of potency. It has the lowest mean inhibitory concentration (MIC) for most bacterial endophthalmitis isolates<sup>13</sup>; thus, it seems to be a better choice for prophylactic antibiotic. The moxifloxacin injection we used was a commercially available ophthalmic solution labeled for topical use with the brand name Vigamox. Vigamox does not contain preservatives, which in addition to its broad-spectrum activity led us to investigate its intraocular use. Vigamox has a pH of 6.8 and an osmolality of 290 mOsm/kg; both values are within the compatible range for humans.

Our choice to analyze the data 4 weeks after surgery is supported by observations in previous studies of intracameral instillation of vancomycin, cefuroxime, and cefotaxime<sup>3,23, 24</sup>.

Regarding efficacy, the drug level in the target tissue (in this case the aqueous) becomes paramount. Antibiotic concentrations over time should be established and should be above the MIC<sub>90</sub> levels of the most common, if not all, endophthalmitis-causing pathogens. We injected 0.1mL of Vigamox 0.5% solution, or an equivalent of 0.5 mg (500 mg) of moxifloxacin, into the capsular bag. With an IOL positioned in the capsular bag, the estimated fluid capacity of the combined anterior and posterior chambers after crystalline lens extraction is approximately 0.525 mL.<sup>25</sup> Granting that we reestablished this volume with balanced salt solution (BSS) and the 0.1 mL of antibiotic at the conclusion of the surgery, the concentration of moxifloxacin would be 500 mg in 0.525mL, or 952mg/mL. The median MIC (in mg/mL) of even moxifloxacin-resistant endophthalmitis isolates has been established to be no higher than 3 mg/mL<sup>11</sup>.

Therefore, the initial moxifloxacin levels in the anterior chamber after injection in our cases was at least 300 times the median MICs of endophthalmitis-causing organisms.

So therapeutic levels were achieved peroperatively and it proved to be safe to prevent postoperative anterior chamber reaction and ultimately effective for the prevention of endophthalmitis.

## CONCLUSION

Due to poor socio-economic status in Pakistan, mostly cataract surgery is done by ECCE technique especially in peripheral areas where follow up of such patients is very poor. Moxifloxacin given intracamerally appeared to be nontoxic in terms of postoperative anterior chamber reaction. This study established not only that moxifloxacin can safely be given intracamerally; but also that it is effective in preventing endophthalmitis. So, moxifloxacin given intracamerally is an effective method to prevent drastic complication of endophthalmitis especially in Pakistan.

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