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# Assessment Of Safety Of Prophylactic Intracameral Moxifloxacin In Cataract Surgery

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### **Abstract:**

*Purpose: To assess the safety of prophylactic intracameral Moxifloxacin 0.5% Ophthalmic solution in preventing Post cataract extraction endophthalmitis.*

*Material and methods: The study was conducted at Vijayanagar Institute of Medical Sciences, Bellary, from February 2010 to April 2011. Preoperative and 1-month postoperative anterior chamber reaction was assessed in 50 eyes that had cataract surgery with intracameral moxifloxacin. All patients received 0.1 mL intracameral Moxifloxacin 0.5% ophthalmic solution containing 500 mg of Moxifloxacin at the end of surgery. Patients were assessed for following one month post operatively.*

*Results: 50 eyes completed the study. The mean age was 56 years (range 40 to 70 years). All eyes had quiet anterior chamber preoperatively, later trace to +2 cells and flare anterior chamber reaction on the first day post surgery.*

*Post operative evaluation was done on day 1, one week later and one month later. There was no signs of anterior chamber reaction, decrease in endothelial cell count and changes in corneal thickness was not very significant.*

*Conclusion: Intracameral moxifloxacin 0.5mg/mL appeared to be safe in preventing postoperative anterior chamber reaction with no significant adverse effect on number of endothelial cells, corneal thickness in patients who have undergone extra capsular cataract extraction surgery.*

**Key words:** Intracameral Moxifloxacin, Endophthalmitis, Post operative complications, Cataract extraction, Prophylactic.

### I. INTRODUCTION

Although endophthalmitis is rare but it is a concern for surgeons because the results can be devastating. Endophthalmitis post cataract

extraction has always been a major threat and concern for the ophthalmologists all over the world. Postoperative anterior chamber reaction has been an important predictor for this worst complication. Different antibiotics have been

adopted intracamerally for the prevention of this complication. Among the antibiotics given intracamerally, most commonly used are Cefuroxime and Vancomycin. The medication turn over after intracameral administration is rapid, Moxifloxacin, which is concentration dependent, may be more effective than Cefuroxime, which is time dependent. Before the introduction of Moxifloxacin ophthalmic solution 0.5%, many ophthalmologists used intracameral Vancomycin as part of the prophylactic regime to reduce incidence of post operative endophthalmitis. Although the incidence of endophthalmitis was reduced with Vancomycin, there was no strong proof that Vancomycin prevents post operative endophthalmitis. 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 cystoid macular edema (CME) on fluorescein angiography 1 month and 4 months post cataract surgery. Moreover, because of its higher potency, Vancomycin has been reserved for treatment of infections that are not efficiently manageable by other antibiotics. These doubts and the lack of strong proof of Vancomycin's efficacy in preventing endophthalmitis led to a joint statement by the American Academy of Ophthalmology and the U.S. Center for Disease Control discouraging the routine prophylactic use of Vancomycin in Cataract surgery [6,7]. In a preliminary report of the ESCRS Endophthalmitis Study Group, intracameral cefuroxime was shown

to significantly reduce the risk for developing endophthalmitis post cataract surgery [8]. However, like vancomycin, cefuroxime is available in a systemic preparation and must be reconstituted using saline solution before it can be safely instilled into the eye. This reconstitution of Cefuroxime may increase the risk of Toxic anterior segment syndrome (TASS) if wrong concentration of drug is instilled into the eye.

Considering the possible complications and the effectiveness with Vancomycin and Cefuroxime, intracameral Moxifloxacin seems to be the better choice of antibiotic for prevention of post cataract extraction endophthalmitis because of its broad-spectrum coverage and its mechanism of action. Moxifloxacin is a fourth-generation fluoroquinolone active against a broad spectrum of gram-positive and gram-negative ocular, atypical microorganisms and anaerobes [11,12,13]. The Moxifloxacin ophthalmic solution is isotonic and its pH is 6.8 with an osmolality of approximately 290 mOsm/kg, both values are within the compatible range for humans (pH 6.5 to 8.5 and osmolality 200 to 400 mOsm/kg) reducing the risk for TASS [14,15]. Its commercial ophthalmic formulation which contains no preservatives and can be instilled intracamerally easily. Also in addition, studies in rabbit eyes did not show any intraocular toxicity or reaction following injection of intracameral Moxifloxacin [12].

PATIENTS AND METHOD:

A prospective study comprising of 50 patients was conducted at Vijayanagara institute of medical sciences, Bellary from February 2010 to April 2011 on patients of age 40 to 70 years with no ocular pathology other than cataract. Exclusion criteria included hypermature cataract, glaucoma, retinopathy, maculopathy, corneal opacity or vitreal opacity and visual pathway problems that would cause reduced success rate of postoperative best corrected visual acuity (BCVA). Patients with diabetes, uveitis, corneal endothelial disease or pseudoexfoliation and those who were on systemic immunosuppressants or anticoagulants were also excluded. Other exclusion criteria were intra operative complications or difficulties and prolonged surgery and patients lost in follow up.

Pre operative assessment was done for all 50 patients. Routine ocular examination including nucleus grading (LOCS III), endothelial cell count by specular microscopy and corneal thickness assessment by pachymetry. Pupils were dilated with a Tropicamide 1% eye drops. All surgeries were performed using peribulbar anesthesia of Bupivacaine and Lignocaine. Extra capsular cataract extraction by small incision cataract surgery with implantation of posterior chamber IOL was performed. At the end of surgery, intracameral Moxifloxacin was instilled in each patient. Preoperatively, patient's operating eye instilled with 1 drop of topical Moxifloxacin 0.5% ophthalmic solution every 15 minutes at least 4 times. Povidone-iodine 0.5% was instilled into the cul de sac. On the operating day, the contents

of a newly opened bottle of Moxifloxacin 0.5% ophthalmic solution was drawn into a sterile 10 cc syringe and set aside. With a tuberculin syringe, a volume slightly more than 0.1 mL i-e around 0.3 to 0.5 mL of the pure Moxifloxacin 0.5% ophthalmic solution was then aspirated from the 10 cc syringe. No diluents were added to the commercial preparation. The remaining solution was discarded, keeping 0.1 mL in the tuberculin syringe for instillation into the anterior chamber. The solution prepared in the syringe was injected using a 27-gauge cannula through the incision as the last step of cataract surgery. 0.1ml of Dexamethasone was injected sub conjunctivally and at the end one drop of Moxifloxacin 0.5% ophthalmic solution was instilled topically as well. The procedures for all patients were uneventful with no intra operative complications.

Postoperative antibiotics included Moxifloxacin Ophthalmic solution topically every 2 hourly when patient was awake for first 1week and tapered to every 4hourly for a month. Topical Prednisolone acetate 1% was also given postoperatively using the above dosage schedule used for Moxifloxacin Ophthalmic solution.

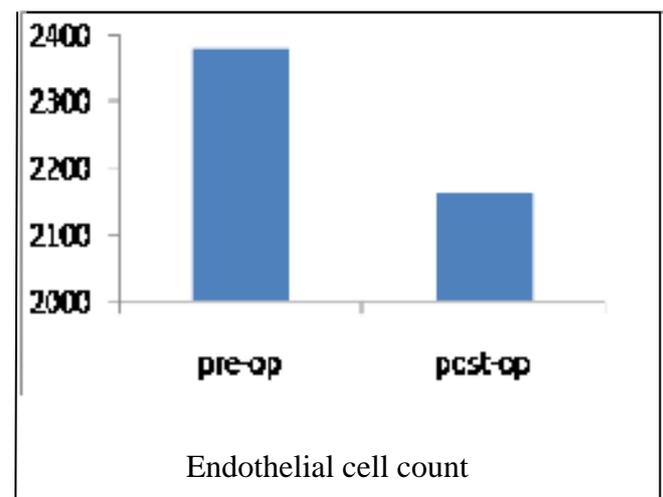
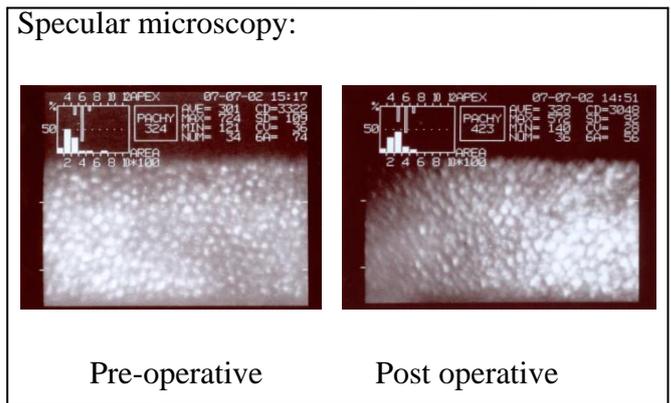
The patients were scheduled for follow-up at 1 day, 1 week, and 1 month post operatively. Visual acuity, anterior chamber reaction, endothelial cell count assessed using non contact specular microscope and corneal thickness measured by Pachymetry. Specular endothelial microscopy of

the cornea was performed with a Non contact specular microscope. Quantitative corneal endothelial cell analysis was done using the variable-frame analysis method. Three images were taken, and the image with the best technical quality was analysed. At least well defined endothelial cells were marked for analysis. Corneal thickness was measured. Anterior chamber reaction expressed as cells and flare intensity, was noted and graded by an independent observer using the Hogan system under slit lamp Biomicroscope.

**RESULT:**

All 50 eyes completed the study with their scheduled follow up. All patients were Indians. The mean age of the 35 men and 15 women was 56yrs (range 40 to 70 years). Most eyes had trace to +2 cells and flare only on the first day post operatively. On subsequent visits, anterior chamber was quiet in 99% (49). Only one patient had anterior chamber reaction on second follow up visit and was given topical steroids frequently, which cured the uveitic reaction. No patient ended up with endophthalmitis at the end of study.

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 safety of injecting intracameral Moxifloxacin in human eyes having cataract surgery to prevent postoperative endophthalmitis.



	pre-op	Post-op
Endothelial cell count	2378	2164
Corneal thickness	0.489	0.503
AC reaction	-	2+
VA	6/60	6/12
Fundus	N	N

**DISCUSSION:**

Endophthalmitis cases post cataract surgery had increased during 1994 to 2001, with a reported

incidence of 2.15 per 1000 cases [18] hence making it necessary for prophylactic protective antibiotics to combat the rise and to treat patients, especially in the light of increasing antibiotic resistance among causative organisms. Among the prophylaxis methods for post cataract surgery, only povidone–iodine was recommended as discussed by Ciulla et al [19] in a literature review of endophthalmitis prophylaxis.

Also Isenberg et al [20] found that povidone–iodine reduces conjunctival flora by 91% for colony-forming units and 51% for species when instilled alone to the eye just before surgery; but when instilled in combination with a topical antibiotic, it produced a synergistic effect that led to sterilization of 83% of the eye. Although antiseptic agents such as povidine–iodine are effective for ocular surface antisepsis, antibiotics with favourable pharmacodynamics are required to provide ocular protection. Then fluoroquinolones were introduced for treatment of corneal and conjunctival infections; but however these antibiotics found a greater role in prophylaxis to prevent endophthalmitis. New generations of fluoroquinolones were introduced to overcome the resistance to the second-generation agents. These include third-generation (Levofloxacin) and fourth-generation (Moxifloxacin and Gatifloxacin) fluouroquinolones. Many studies [11,13,21,22] have proven that Moxifloxacin, a fourth generation antibiotic, is superior in terms of potency. It has the lowest mean inhibitory

concentration (MIC) for most bacterial endophthalmitis isolates[13]; also Moxifloxacin has been found to penetrate the eye significantly better than

Ofloxacin; thus making it a better choice for prophylaxis.

Moxifloxacin ophthalmic solution is devoid of preservatives, which in addition to its broad-spectrum activity, made to investigate its intraocular use. It has a pH of 6.8 and an osmolality of 290 mOsm/kg and both these values are within the compatible range for humans.[14]

We assessed the biocompatibility of this antibiotic by

observing its effects on the cornea (endothelial cell count and pachymetry) and blood–aqueous barrier (BAB) (aqueous flare) and whether it caused anterior chamber reaction (aqueous cells). We found no statistical evidence of reduced endothelial cells or increased corneal thickness in our patients as early as 4 weeks postoperatively compared to preoperatively. The 9% endothelial cell loss in our study group is comparable to that in most studies, which report a mean reduction in endothelial cells after cataract surgery ranging from 4% to 15%. [23] In addition, we found no proof that Moxifloxacin causes increased BAB disturbance or secondary reaction, which would have caused raised aqueous flare levels and raised cell levels, respectively. All eyes had no anterior chamber reaction at the 1-week postoperative

follow-up visit. No eye lost a line of BCVA from the preoperative acuity.

Our choice to analyze the data 4 weeks after surgery is based on previous studies of intracameral instillation of Vancomycin, Cefuroxime, and Cefotaxime [3,24–26] Kramann et al.[26] report no further postoperative loss of endothelial cells after 4 weeks, which suggests wound healing is completed by that period. Cheng et al.[27] and Amon et al.[28] report that preoperative corneal thickness values were restored within a similar period of time with only Povidone iodine prophylaxis, incidence of endophthalmitis is 0.3-0.5% in Europe [16, 17] and 0.015% in USA. While in India this rate was found to be 0.05% [6].

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 [9] . Thus, there is a need for protective antibiotics to combat the rise and to treat patients, especially in the light of increasing antibacterial resistance among causative organisms.

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 levels of the most common, if not all, endophthalmitis-causing pathogens. We injected 0.1mL of Moxifloxacin 0.5% ophthalmic solution 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 [25]. Granting that we re-established 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 3mg/mL [11].

Hence 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 pre operatively and it proved to be safe to prevent in prevention of endophthalmitis.

Development of resistant strains through mutation with the prophylactic use of antibiotics was another parameter to be evaluated for antibiotic potency. This drug level is called the mutant prevention concentration (MPC), which addresses the concern that frequent, suboptimal use of antibiotics increases the chances for and hastens the appearance of resistant mutant strains. Knowing and more importantly achieving, the concentrations above these levels more or less ensures prevention of such strains. The MPC of Fluoroquinolones is typically 8 to 10 times their MIC [30,31] .Calculations show that the Moxifloxacin concentrations initially achieved in our patients were at least 30 times the estimated

MPCs of the antibiotic for endophthalmitis isolates.

Another issue is the antibiotic's concentration in the anterior chamber over time and its effective kill rate. Unfortunately, there is less data in the literature on the bioavailability of antibiotics after intraocular administration in humans. [32] Furthermore, the data in these studies are not entirely conclusive as a result of unavoidable limitations in aqueous humor sampling. Because of the small volume of aqueous, which prevents repeated extractions, these studies evaluated antibiotic concentrations in different patients at different times. Still, these provide only a general idea of aqueous humor clearance and of the concentrations of intraocularly administered medications over time. One study estimates a decline in aqueous humor antibiotic concentration by a factor of 4 in 1 hour [24]. The investigators, however, instilled the antibiotic (cefuroxime) in a non-distended anterior chamber to avoid overfilling the chamber and prevent leakage of the antibiotic solution. The actual half-drop in concentration, however, may be closer to 1 to 2 hours, as reported for irrigation fluid antibiotics. [32] If these data reflect actual circumstances and if presumed constant elimination rates based on available information are to be believed Moxifloxacin levels in the aqueous exceeding MICs for relevant species will persist for a conservatively estimated time of 5 hours. Mutant prevention concentrations, on the other hand, will be

maintained until approximately 3 hours after surgery.

#### CONCLUSION :

India is a developing nation and mostly cataract surgery is done by ECCE technique but follow up of patients especially in peripheral areas is not satisfactory. Moxifloxacin given intracamerally appeared to be nontoxic in terms of postoperative visual rehabilitation, anterior chamber reaction, pachymetry and corneal endothelial cell density. This study established not only that Moxifloxacin is safe when given intracamerally but also that it is very effective in preventing post-operative endophthalmitis. So, Moxifloxacin given intracamerally is an effective method to prevent drastic complication of endophthalmitis especially in developing countries like India.

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