



## **A CLINICAL COMPARISON OF THE EFFICACY & PENETRATION OF MOXIFLOXACIN AND LEVOFLOXACIN IN CATRACT SURGERY CASES**

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### **ABSTRACT**

A cataract is the clouding or opacity of the normally clear, natural crystalline lens of the eye, which lies behind the iris and the pupil. There are an established 9-12 million blind in India, half of which can be attributed to cataract. Endophthalmitis is a potentially sight threatening complication of cataract surgery. Fluroquinolones penetrate vitreous better than other antibiotics and is used by many clinicians, but have not been suggested to rigorous, blinded clinical trials.

**Objectives:** The main objective of this study is to compare the efficacy and penetration ability of topically applied 0.5% Moxifloxacin and 0.5% Levofloxacin ophthalmic solutions into human aqueous humor before routine cataract surgery.

**Materials and Method:** Microbiological study was carried out on patients' conjunctival smear before and after administration of antibiotic. Fifty patients that underwent cataract extraction were divided randomly into two groups with Moxifloxacin (25 Patients) and Levofloxacin (25 Patients).

**Result:**Based on the penetration study, the mean concentration of Moxifloxacin in the aqueous humor was significantly greater than that of Levofloxacin in both types of regimens namely regime A and B. The MIC<sup>90</sup> value of Moxifloxacin was found to be lower than that of Levofloxacin for most key ocular pathogens.

**Conclusion:**This study provides an evidence based conclusion that cataract surgery can be done as an out patient procedure without any complication to the patients and that Moxifloxacin has a better penetrating power than Levofloxacin in the aqueous humor.

**Keywords:** Moxifloxacin, Levofloxacin, Endophthalmitis.

### **INTRODUCTION**

A cataract is the clouding or opacity of the normally clear, natural crystalline lens of the eye, which lies behind the iris and the pupil. Cataract is the chief cause of preventable blindness all over the world, according to the world health organization.<sup>1</sup> Cataract ranks only behind arthritis and heart disease as a leading cause of disability in older adults.

There are an established 9-12 million blind in India, half of which can be attributed to cataract. A huge backlog of cataract blindness exists in the developing world.<sup>2</sup> It is estimated that 3.8 million people develop blinding cataract every year in India,<sup>3</sup> as against 2.7 million cataract surgeries done every year.

The common symptoms are blurring of vision, glare, change in colour of vision, double images, necessity for frequent change of glasses. The types of cataracts are Senile Cataract, Nuclear Cataract, Cortical Cataract, Posterior Subcapsular Cataract, Congenital Cataract, Secondary Cataract, Traumatic Cataract. The only effective treatment for a cataract is surgery to remove the clouded lens, which usually includes replacing the lens with a clear lens implant. Sometimes cataracts are removed without reinserting implant lenses. In such cases, vision can be corrected with eyeglasses or contact lenses.

Cataracts can't be cured with medications, dietary supplements, exercise or optical devices. In the early stages of a cataract when symptoms are mild, a good understanding of the condition and a willingness to adjust your lifestyle can help. Some self-care approaches, such as using a magnifying glass to read or improving the lighting in your home, may help you deal with the effects of having a cataract<sup>4</sup>.

Endophthalmitis is an ocular inflammation resulting from the introduction of an infectious agent into the posterior segment of the eye. During infection, irreversible damage to delicate photoreceptor cells of the retina frequently occurs. Despite aggressive therapeutic and surgical interventions, endophthalmitis generally results in partial or complete loss of vision, often within a few days of inoculation<sup>5</sup>.

The choice of prophylactic topical antibiotic and the optimal dosing regimen are subject to debate. An important consideration is whether the preoperative administration of a topical antibiotic result in drug concentrations in the aqueous humor that is greater than the minimum inhibitory concentration (MIC) for potential bacterial pathogens<sup>6</sup>. Additionally, the medication chosen should have a broad spectrum of antimicrobial activity particularly against gram-positive organisms, cause no corneal toxicity, and have excellent solubility (bioavailability) so that it readily penetrates the tissues of the eye. Topical fluoroquinolones have been shown to be efficacious and well tolerated for the treatment of bacterial conjunctivitis<sup>7,8</sup>. Fluoroquinolones are also being used for prophylaxis in ocular surgery.

Accordingly, in a survey of ophthalmologists performing cataract surgery in 2000 in the United States, 79% reported use of a preoperative topical antibiotic<sup>9</sup>. Ophthalmic surgeons commonly prescribe antibiotic for topical dosing 2 or 3 days before or pulse dose in the operating room immediately before surgery.

This work has been necessitated due to the rising complications of endophthalmitis and in the search to find the best fluoroquinolone available in the market based on efficacy and penetration.

### **MATERIALS AND METHODS**

**Study design:** A prospective, double-masked, parallel, randomized, case control study.

**Study site :** Vasan Eye Care Hospital, Tiruchiappalli.

**Study period:** The study was conducted during a six month period.

### **Inclusion/exclusion criteria:**

The subjects of either sex (otherwise healthy) who were scheduled to undergo standard cataract surgery, 21years of age or older, had the ability to understand and give signed informed consent were included.

Those that exhibited any intraocular inflammation, was a subject using any ocular medication or drops 48 hours before or during the study period (other than the study treatment), had a known

sensitivity to any of the ingredients in the study medications or any quinolone compound, had a condition that may confound the study results, or may interfere significantly with the subject's participation in the study, had abnormal eyelid function, had only one eye, would require the use of any systemic antibiotic during the study period, was exhibiting a corneal ulcer, keratitis, or had a history of herpetic keratitis, had any ocular disease that would interfere with the evaluation of the study treatments, received previous intraocular silicone oil, was pregnant or nursing were excluded.

### Method of the study

The clinical ethics committee of the institution approved of the study. The 50 patients undergoing cataract extraction were divided randomly into two groups with 0.5% Moxifloxacin -25 patients and 0.5% Levofloxacin -25 patients.

Three days before surgery the patient's conjunctival smear was taken as a baseline. Then the assigned drug was given randomly to each patient at a dose of a drop four times a day for three days. After three days of administration at the time of surgery a second smear was taken to assess the bacterial load to find the efficacy of the drugs.

Conjunctival swab material was inoculated into 0.3 ml of sterile saline in a sterile vial. The swab was repeatedly twirled in the saline. In the laboratory, 0.1ml of the saline was inoculated onto a plate of 5% sheep blood agar while 0.05 ml each was inoculated onto a plate of cystine-tryptone-agar and a plate of MacConkey agar.

Following inoculation, the plates were incubated in a bacteriological incubator at 37°C and after overnight incubation and after 48 hours the plates were checked. If bacterial growth was obtained on the plates, the colony count was first estimated by counting the number of colonies in the streaked area of the plate and multiplying the same by 10. A smear of an individual colony was prepared on a microscope slide, and this was stained by the gram method, dried and viewed under the oil immersion objective or a light microscope. If positive, with the presence of beta haemolysis on blood agar and growth on MacConkey agar, the growth was considered to be *staphylococcus aureus*. If coagulase test was negative, with no beta haemolysis on blood agar and no growth on MacConkey agar, the growth was considered to be a coagulase-negative staphylococcus.

### Penetration (Aqueous)

The patients were instructed to use their antibiotic drops according to regimen A or B to which they were assigned.

Regimen A: 1 drop four times a day for three days (12 drops) -23 patients and

Regimen B: 1 drop - 6 doses delivered every 10 min in the hour immediately preceding surgery (6 drops)-15 patients.

During surgery 0.2 ml of aqueous fluid was aspirated with the help of a tuberculin syringe. The anterior chamber fluid was immediately placed into a sterilized cryogenic tube and stored at -40° C in an Ultra Low Freezer (Remi®, Remi Instruments, Mumbai) and kept frozen until analysis was performed. Each tube was marked with a patient identification number (which indicated the antibiotic that the subject was randomly assigned), the subject's initials, date of surgery, and eye. Concentrations of topically applied fluoroquinolones were determined by use of reverse-phase high-pressure liquid chromatography assay technique with ultraviolet-visible detector at a wavelength of 275 nm.

### Moxifloxacin and Levofloxacin

#### Chromatographic Conditions

Stationary Phase :Gemini 5u C18 (2) 100A 250 x 4.60 mm

Mobile Phase :Acetonitrile: Phosphate buffer (pH 5)

Mobile phase ratio :20: 80 % v/v

Flow rate :1.0 ml/min

Sample volume :20µl

Detection :275nm using UV Visible detector.

Data station :Class VP data station

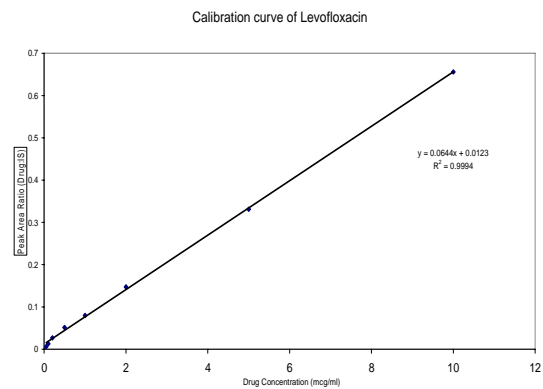
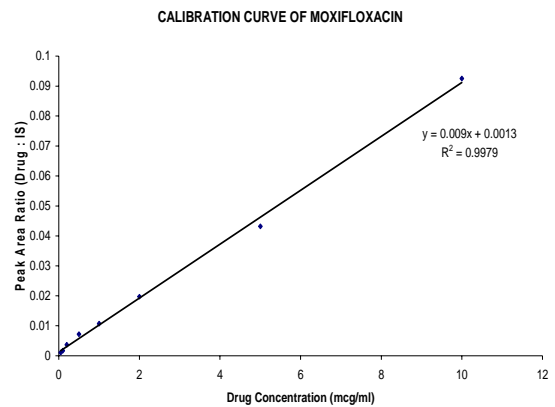


Table 1: Mean VALUE representation of levofloxacin and Moxifloxacin

Dosing regimen	Levofloxacin (µg/ml)	Moxifloxacin (µg/ml)
A	0.18 ±0.05 (n = 8)	0.77 ±0.15 (n = 15)
B	1.34 ±0.33(n = 9)	1.94 ±0.06 (n = 6)

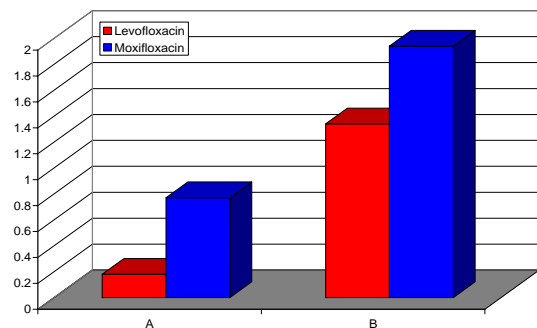


Fig. 1: Bar Graph

### Statistical methods

The collected data were subjected to statistical analysis and results analysis was done by using Anova test.

## RESULTS

The average age of the 50 patients under study was 60.52 years. Male patients numbered 32 (64%) and female patients numbered 18 (36%). Among this the patients having associated disease of diabetes alone 22 (44%), hypertension alone 18 (36%) both hypertension and diabetes were 9 (18%), and patients with anemia 25 (50%). Microorganisms isolated were *Staphylococcus aureus* in 21 (42%) patients, *Staphylococcus epidermidis* in 18 (36%) patients.

## DISCUSSION

Amongst 50 patients undergoing cataract extraction were divided randomly into two groups with 0.5% Moxifloxacin – 25 patients and 0.5% Levofloxacin – 25 patients. Three days before surgery the patients' conjunctival smear was taken to find the bacterial load as a baseline. Then the assigned drug was given to each patient at a dosage of 4 times a day for three days.

After 3 days of administration a second smear was taken and there was no growth in both the groups. So both the drugs were found to be effective on the surface as a prophylactic prior to phacoemulsification. In the microbiological aspect of this study, the two antibiotics Levofloxacin and moxifloxacin were effective in eradicating the bacterial flora from the conjunctiva after 3 days of drug administration. Both the drugs registered no growth after drug treatment.

The new generation of fluoroquinolones addresses the problem of emerging bacterial resistance with a broader spectrum of activity<sup>10-14</sup>. The most recent therapeutic agents include the fourth-generation fluoroquinolone moxifloxacin 0.5%. Unlike prior generation fluoroquinolones that predominantly inhibit topoisomerase IV or DNA gyrase and, therefore, only require 1 genetic mutation for bacteria to develop resistance,<sup>15</sup> fourth-generation fluoroquinolones work on both bacterial DNA gyrase and topoisomerase IV<sup>16,17</sup>. To become resistant to these agents, the bacteria must undergo 2 genetic mutations, resulting in a significantly decreased chance of an organism developing resistance<sup>18</sup>.

The increased efficacy of fourth-generation fluoroquinolones against gram-positive organisms<sup>19, 20</sup> makes these antibiotics important agents to evaluate for prophylaxis against post cataract surgery endophthalmitis.

In this study we have found that the mean concentration of Moxifloxacin in the aqueous humour was significantly greater than that of Levofloxacin in all the treatment groups ( $p < 0.0001$ ).

In the regimen A, the mean  $\pm$  SD for Moxifloxacin was found to be  $0.77 \pm 0.15$  ( $n = 15$ ) and that of Levofloxacin it was  $0.18 \pm 0.05$  ( $n = 8$ ). This represented a 4.28 fold difference in measured aqueous humor antibiotic concentration which was statistically significant ( $p < 0.001$ ).

In the regimen B, the mean  $\pm$  SD for Moxifloxacin was found to be  $1.94 \pm 0.06$  ( $n = 6$ ) and that of Levofloxacin it was  $1.34 \pm 0.33$  ( $n = 9$ ). This represented a 1.45 fold difference in the antibiotic concentration which was considered to be statistically significant ( $p < 0.001$ ). Regimen B delivered more drug in the aqueous than Regimen A for both the drugs. In Moxifloxacin there was 2.52 fold difference ( $p < 0.001$ ) and for Levofloxacin there was 7.44 fold difference ( $p < 0.001$ ) mean values were shown in the Table 1 and graphical representation shown in figure 1.

No clinically evident epithelial or intraocular toxicity was noticed with the topical application of any of the antibacterial agents used in this study.

The strengths of this study include that it was prospective and double-masked. The limitations of the study include small and uneven sample sizes and difficulty in flawlessly evaluating preoperative antibiotic compliance.

## CONCLUSION

It is concluded that there was no difference between Moxifloxacin and Levofloxacin ophthalmic solution on the conjunctival flora since both the drugs were effective in eradicating the bacteria from the

surface. But for a drug to be used as a prophylactic prior to intraocular surgery continuous MIC levels must be present in the aqueous and vitreous to prevent postoperative endophthalmitis. So the drug should have a good penetration.

Based on the penetration the mean concentration of Moxifloxacin in the aqueous humor was significantly greater than that of Levofloxacin in both the regimes A and B.

Regimen B delivered more drug in the aqueous humor than Regimen A with both the drugs. In moxifloxacin there was 2.52 fold difference ( $p < 0.001$ ) and for Levofloxacin there was 7.44 fold difference ( $p < 0.001$ ). The fourth generation fluoroquinolone eye drops have been developed to broaden the spectrum of antibiotic coverage, including resistant strain.

So we can come to an evidence based conclusion that cataract surgery can be done as an out patient procedure without any complication to the patient by using regimen B and Moxifloxacin was found to have a better penetration than Levofloxacin in the aqueous humor.

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