

## Safety of Prophylactic Intracameral Moxifloxacin during Phacoemulsification

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**Abstract: Aim of the work:** To evaluate the safety of Intracameral moxifloxacin during standard coaxial phacoemulsification. **Subjects and Methods:** a prospective randomized controlled clinical trial. Sixty patients with 60 eyes were divided into two Groups: **Group 1:** Vigamox group (30 eyes), **Group 2:** Control group (30 eyes) Injection of 0.1cc Moxifloxacin using insulin 30G syringe in group 1 were done at the end of Standard coaxial phacoemulsification with Foldable IOL. **Results** The mean age was  $64.2 \pm 7.8$  years. The preoperative VA range from HM to 6/12 which changed postoperatively as mostly improved more than 6/18 with a total lines gained up to 12 lines. The intraoperative complications, were few in which 4 eyes showed posterior capsular dehiscence, 1 eye with Positive Vitreous Pressure (3.3%) & one case of Vitreous Prolapse (3.3%). Post-operative complications was corneal edema which was slightly more in vigamox group than that occurring in the control group, corneal edema occurred in 8 cases in the vigamox group and 6 cases in the control group, 5 cases suffered from Suture-Induced Astigmatism. Unfortunately there was one case suffered from endophthalmitis, one with Pupillary Block, one with Retained Lens Material, one case of media opacity, also one case with Shallow Anterior Chamber. The average endothelial cell density in the control group was 2366.75 and changed to 2083.75. While the average endothelial cell density in the vigamox group was 2533.21 then one month postoperatively changed to 2006.29 meaning that there was a decrease of 283 in the control group compared to the 526.93 decrease in the vigamox group. **Conclusion:** Intracameral 0.1 ml of 0.5% moxifloxacin (Vigamox, Alcon) was found to be safe for the visual rehabilitation and corneal endothelium. Use of Intracameral moxifloxacin can be a beneficial adjunct to topical dosing for surgical prophylaxis.

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**Key words:** Intracameral Moxifloxacin, vigamox, endophthalmitis

### 1. Introduction

The use of prophylactic antibiotics in elective cataract surgery remains controversial. Despite a lack of evidence that these agents prevent postoperative infection, many cataract surgeons routinely administer intracameral antibiotics to avert the potentially devastating outcomes of endophthalmitis<sup>1</sup>.

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>2</sup>

Endothelial toxicity leading to corneal decompensation is another severe complication of cataract surgery. Often iatrogenic as a result of mechanical or chemical insult to the endothelium, endothelial toxicity is related to the chemical

composition, concentration, pH, and osmolality of substances that come in contact with the endothelium and may lead to irreversible corneal edema. Some cases of TASS also result in localized corneal endothelial damage.<sup>3</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. Moxifloxacin is a fourth-generation fluoroquinolone antibacterial agent that is active against a broad spectrum of gram-positive and gram-negative ocular pathogens, atypical microorganisms, and anaerobes.<sup>3,4,5</sup> 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, ); both values are within the compatible range for humans (pH 6.5 to 8.5 and osmolality 200 to 400 mOsm/kg).<sup>5,6,7</sup> 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. In addition, early studies of rabbit eyes did not show intraocular toxicity after injection of intravitreal or intracameral moxifloxacin.<sup>3</sup>

#### **Aim of the work**

Aim of this study is to evaluate the safety of Intracameral moxifloxacin during standard coaxial phacoemulsification as regards visual rehabilitation, anterior chamber reaction, corneal endothelial cell density, pachymetry

## **2. Subjects and Methods**

### **Patient Selection**

This is a prospective randomized controlled clinical trial. Patients included in this study were 60 with 60 eyes. The patients were selected from the outpatient clinic.

They were examined, investigated and followed up from 2009 to 2010 with follow up period of 6 months for 40 cases who complete the study protocol. The other 20 patient from the control group didn't have a complete data for the specular microscopy.

### **Inclusion criteria**

All cases of senile cataract without local or systemic diseases that may affect the endothelial cell count.

### **Exclusion criteria:**

1. Patients with cataracts other than senile will be excluded.
2. Patients with endothelial cell count less than 2000/mm<sup>2</sup>
3. Patients with detectable retinal or optic nerve lesions.

### **Patient examination**

**History:** personal, past, present and family history was taken for every patient. History of previous ocular surgery was recorded.

Complete ophthalmological examination of both eyes was done by the Slit lamp. Vision was tested unaided and aided by Snellens chart. IOP was measured by applanation tonometry

### **Patient investigations**

As for any cataract extraction operation PC IOL calculation were done by IOL master and posterior segment ultrasonography when needed to exclude posterior segment pathology if media were not clear. Preoperative specular microscopy using the non contact Konan specular microscopes was done as well as one month post operatively to examine the effect of intracameral injection of vigamox at the end of phaco procedure on the cornea

### **Patients were divided into two Groups:**

**Group 1:** Vigamox group ( 30 eyes)

**Group 2:** Control group ( 30 eyes)

Standard coaxial phacoemulsification with insertion of Foldable IOL were done to all patient in which injection of 0.1cc taken from newly opened bottle of vigamox eye drop using insulin 30G syringe in group 1 were done after corneal hydration of the wound.

### **Postoperative care and Follow Up**

Patient's post-operative regimen include topical antibiotics and steroids

All patients were examined post operatively for at least 9 visits (day 1, day 3, day 7, 2 weeks, 3 weeks, 1 month, 2, 4 & 6 months).

All the patients were examined by Slit lamp for corneal clarity, anterior chamber activity, intraocular pressure and configuration of the pupil were recorded. also Visual acuity measured and corrected. Specular microscopy was done for all vigamox group but for only 10 patients of the control group using the Konan Specular microscope in the Diagnostic and Laser Unit in Kasr El Aini Hospital, Cairo University.

### **3.Results**

Collected patient data include 30 patient data in the vigamox group and 30 patients in the control group. Twenty patients' data was excluded from the statistical analysis of the Specular microscopy due to incomplete data

We analyzed the data of 60 patients with 60 eyes. Collected data were entered into an excel sheet and stored in excel format using Microsoft Excel 2010.

The data collected and analyzed using the Microsoft office 2010 using the excel sheets for data entry and statistical analysis and graph drawing. Also the Statistical package for social science (SPSS) software version 17 was used in some tests.

The mean age was  $64.2 \pm 7.8$  years for the patients included in the study as shown in table 1. The demography showed that 53 % of the patients were female in both groups while the rest 47% were males as shown in table 1

**Table 1: age distribution of group**

		Group		
Sex	Data	Control	Vigamox	Total
Female	no	16	17	33
	Mean± SD	62.9±	62.6±	62.8±
Male	no	14	13	27
	Mean ±SD	63.6±	68.4±	65.9±
Total no		30	30	60
Mean ±SD		63.3±	65.1±	64.2±

Complete ophthalmological examination of both eyes was done by the Slit lamp. There were 26 right eyes (n=11 control & n=15 vigamox) and 34 left eyes (n=19 control & n=15 vigamox)

For all patients both anterior and posterior segment examination was done in which anterior segment examination was within normal. Lens examination revealed posterior sub capsular cataract of 17 patients that were dense enough to make best corrected visual acuity to be up to counting finger but the rest ranging in density from faint to different densities. The rest were nuclear grade 2 till 4 as well as cortical mature and immature cataract as shown in table 2

**Table 2: preoperative lens findings in both groups**

Lens	Control	Vigamox	Grand Total
IMSC	6	6	12
MSC	7	1	8
Nuclear II	6	5	11
Nuclear III	2	6	8
Nuclear IV	2	2	4
Post SubCap	7	10	17
Grand Total	30	30	60

Vision was tested unaided and aided with preoperative BCVA ranging from HM to 6/12 for both groups

IOP was measured by applanation tonometry which was ranging between 9 & 20 mmHg except for 2 patients with ocular hypertension reaching up to 23 and 25 mmHg respectively. The mean IOP was  $15.0 \pm 3.0$  mmHg

Fundus examination with mydriatic was performed in which most of fundi were normal fundi or tigroid (n=43) while the rest were myopic n=8, and 9 were hazy

As for C.D. ratio there were 33 patients couldn't evaluate their CD ratio due to the hazy view of the fundus. Most of the patients fall between 0.0 & 0.4 except for 4 patients were having large physiological C.D. ratios as evidenced by non significant visual field changes.

#### **Patients were divided into two Groups:**

Group 1: Vigamox group ( 30 eyes)

Group 2: Control group ( 30 eyes)

All patients in the study complete the 6 month follow up period.

**The post-operative results showed that First Visit VA, was 3/60 or more**

Slit Lamp Examination (SLE): corneal edema proportional to ultrasound time for control group but slightly more in Vigamox group. Eight patients

showed moderate corneal edema and two cases showed severe corneal edema.

For these two cases, Hydrocortisone 1% eye ointment was added twice daily till corneal edema resolved which took around two weeks.

- 1-2+ cell and flare for control group and 3-4+ cells and flare for Vigamox group

IOP: was measured digitally in first post operative day and those with higher IOP were given antiglaucoma treatment. All cases showed relative red reflex.

#### **Second Visit (day 3)**

Improvement of BCVA in all patients with decrease of corneal edema and also slight decrease in cells and flare

#### **Week #1**

Post operative refraction was done to correct post operative refractive errors

#### **Slit Lamp Examination**

Little corneal edema and trace to 0/1+ cell and flare for control group and 1/2+ cell and flare for Vigamox group

#### **Fundus Examination**

Fundus exam was within normal

#### **Week 2**

BCV.A. increased as expected.

No corneal edema and clear A.C. for both control group and Vigamox group.

One case from the control group showed increase in flare and cells with hypopyon and signs of endophthalmitis as evidenced by ultrasound which showed moderately dense dispersed vitreous opacities. Vancomycin and Fortum subconjunctival injections were given every 24 hours and I.V. infusion 12 hourly as well as, atropine drops, chloramphenicol, Ofloxacin, tobramycin, orchacin eye drops every 30 minutes successively until complete resolution of endophthalmitis signs.

Patients continue on antibiotic eye drops after complete resolution of endophthalmitis for ten days then signs of recurrent endophthalmitis were detected where readmission to the hospital with the same medical treatment until complete resolution of endophthalmitis then core vitrectomy was done to remove post endophthalmitis membranes and PCO.

#### **Week 3, week 4, 2 months, 4 months & 6 months:**

Resolution of all flare and cells as well as corneal edema.

#### **Start of late post operative complications.**

#### **IOP changes**

The mean IOP was  $15.02 \pm 3.17$  mmHg preoperatively which was decreased to  $13 \pm 3.31$  mmHg postoperatively with a difference of  $-2.875 \pm 3.58$  mmHg. The IOP ranged from 9-25 mmHg preoperative and from 5-18 mmHg postoperative.

#### **Visual acuity**

The preoperative VA range from HM to 6/12 This changed postoperatively in which mostly improved more than 6/18 with a total lines gained up

to 12 lines and least of a deterioration of one line which occurred with one case as well as with the endophthalmitis case. This was shown in the table 3.

**Table 3: summary of the BCVA postoperatively**

Vision	Control	Vigamox	Total	%
More than 6/18	25	22	47	78.33%
6/60-6/24	3	6	9	15.00%
Less than 6/60	2	2	4	6.67%

#### Intraoperative complications

The intraoperative complications, were few in which 4 eyes showed posterior capsular dehiscence, 1 eye with Positive Vitreous Pressure which account

for 3.3% in the control group, one case of Vitreous Prolapse (3.3%) and there were no report of Expulsive Hemorrhage, Descemet's Detachment or Wound Mal apposition as shown in table 4.

**Table 4: Intraoperative complications for both groups**

Intraoperative complications	Vigamox		Control	
	n	%	n	%
Posterior Capsular Dehiscence or Zonular Dialysis	2	6.7%	2	6.7%
Positive Vitreous Pressure	0	0.0%	1	3.3%
<i>Vitreous Prolapse</i>	1	3.3%	0	0.0%

#### Early post-operative complications

The most common early post-operative complications was corneal edema which was slightly more in vigamox group than that occurring in the control group, corneal edema occurred in 8 cases in the vigamox group and 6 cases in the control group, 5 cases suffered from Suture-Induced Astigmatism. Unfortunately there was one case suffered from endophthalmitis, one with Pupillary Block, one with Retained Lens Material, one case of media opacity, also one case with Shallow Anterior Chamber But there was no Wound Leak, Choroidal Detachment,

Iris Prolapse, Postoperative Uveitis, Optic Nerve abnormalities or, Post-Refractive Subnormal Vision as shown in table 5 and Figures 1&2. Figures 1&2 show the corneal oedema for both groups in the early postoperative follow up visits.

#### Late postoperative complications

The most common late post-operative complications was posterior capsule opacification occurring in 19 cases, 7 eyes showed Change in Refraction, one case suffered from Cystoid Macular Oedema and another showed uveitis. No other late complications were detected. as shown in table 6

**Table 5: Early postoperative complications for both groups**

<i>Early postoperative complications</i>	<i>Vigamox</i>	<i>Control</i>
Shallow Anterior Chamber		1
Wound Leak		
Pupillary Block	1	
Choroidal Detachment		
Iris Prolapse		
Postoperative Uveitis		
Infectious Endophthalmitis		1
Corneal Oedema	8	6
Retained Lens Material		1
Suture-Induced Astigmatism	2	3
Post-Refractive Subnormal Vision		
Media Opacities		1
Retinal Pathology	1	1
Optic Nerve abnormalities		



**Figure 1: Second day postoperative severe corneal haze in vigamox group**



**Figure 2: Second day postoperative corneal haze in control group**

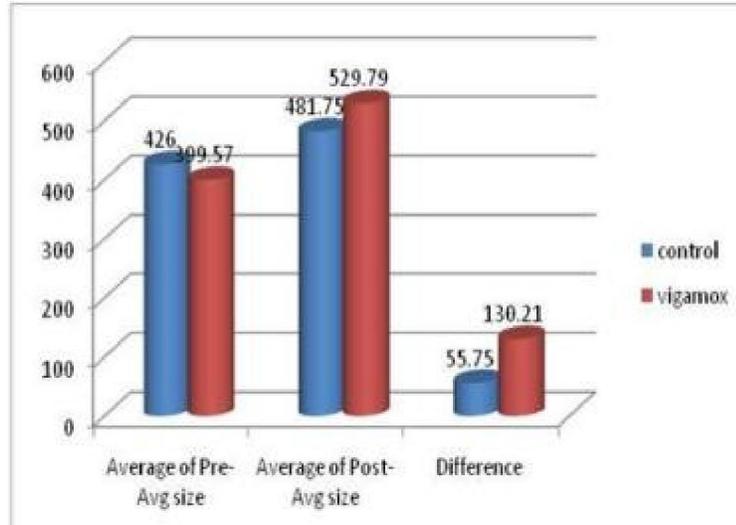
**Table 6: Late postoperative complications for both groups**

<i>Late postoperative complications</i>	<i>Vigamox</i>	<i>Control</i>
Change in Refraction	4	3
Posterior Capsule Opacification	9	10
Cystoid Macular Oedema	1	
RD		
loose sutures,		
Uveitis,		1
Chronic irritable eye,		
Epithelial downgrowth		
Bullous keratopathy.		

**Specular Microscopy Results:**

The average preoperative endothelial cell size was within 400 microns however there was an increase in average cell size in both groups. In the

control group there was a difference of 55.75 m compared to that of the control group which was 130.21m as shown in figure -3.



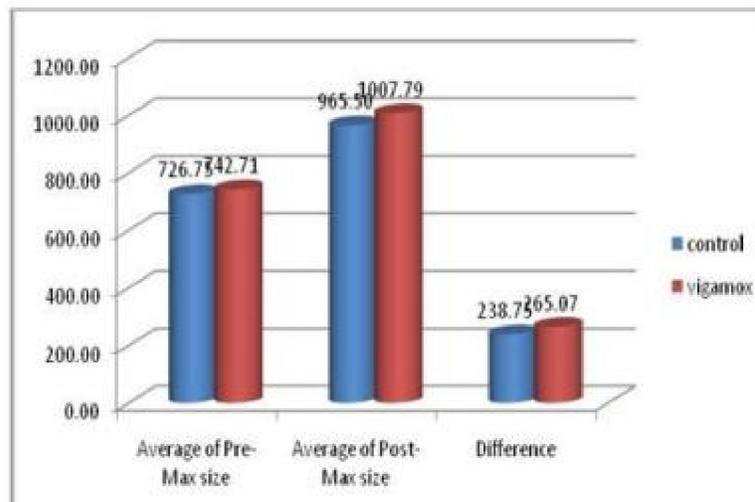
**Figure 3: Demonstrating the average endothelial cell size and their difference.**

The maximum cell size for both groups preoperatively was with an average of 700m while the post operative maximum cell size reached 965.50m with a difference of 238.75 in the control group compared to the vigamox group which showed an average increase in the maximum cell size reaching 1007.79 with a difference of 265.07 as shown in figure 4.

On comparing the average minimum cell size for both groups the preoperative minimum cell size was 160m which almost didn't change postoperatively for the control group but which increased to 205.29 in the vigamox group with a difference of 44.64m this is demonstrated in the figure 5.

The preoperative average endothelial cell count was 27.75 in the control group which decreased to 27 one month postoperatively compared to the vigamox group which was 29.5 preoperatively and decreased to 25.43 postoperatively as shown in figure 6. Showing that there was a decrease of 0.75 in the control group and a decrease of 4.07 in the vigamox group as shown in figure 6.

The average endothelial cell density in the control group was 2366.75 and changed to 2083.75 as shown in figure 7. While the average endothelial cell density in the vigamox group was 2533.21 then one month postoperatively changed to 2006.29 as shown in figure 7. meaning that there was a decrease of 283 in the control group compared to the 526.93 decrease in vigamox group as shown in the figure 7.



**Figure 4: showing, The maximum cell size**

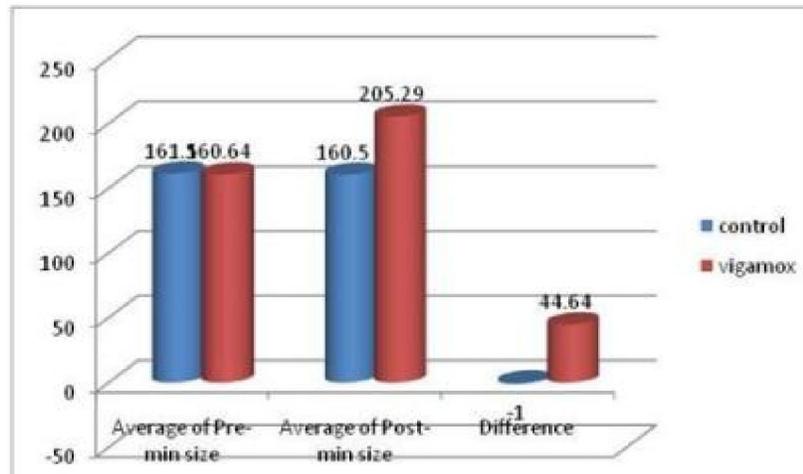


Figure 5. The differences in the average minimum cell size between pre and post-operative changes in both groups.

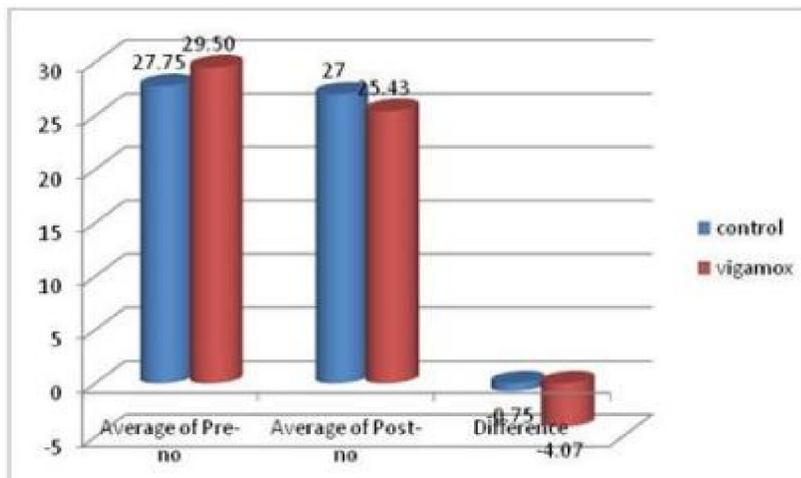


Figure 6. The average endothelial cell count in both groups.

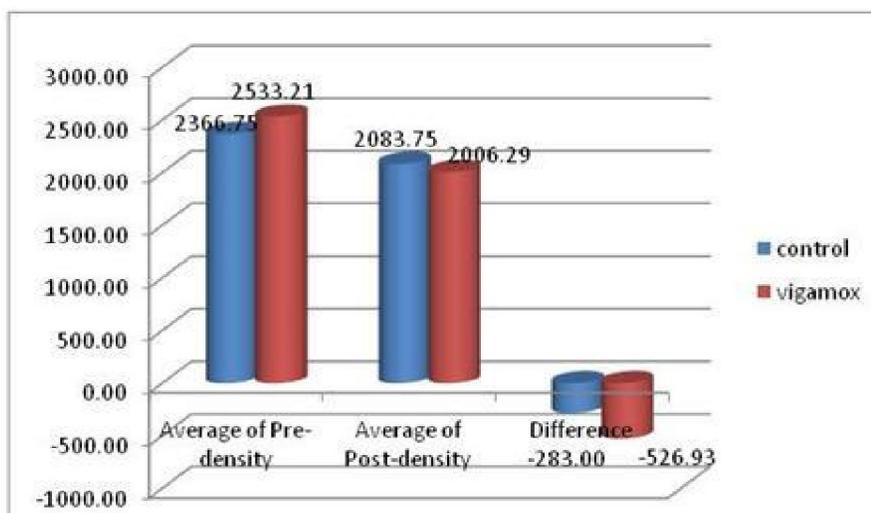


Figure 7. The average endothelial cell density in both groups.

The average preoperative standard deviation in the control group was 145.50 and changed to 193.75 one month postoperatively as shown in figure 8.

While the average standard deviation in the vigamox group was 137.36 preoperatively and changed to 200.14 as shown in figure.8

The difference in the average standard deviation in the control group was 48.25 compared to the vigamox group which was 62.79 as shown in figure.8

The average preoperative coefficient of variation in the control group was 33.75 and changed to 39.75 one month postoperatively as shown in figures 9.

While the average coefficient of variation in the vigamox group was 33.86 preoperatively and changed one month postoperatively into 36.36 as shown in figure. 9.The difference in the average coefficient of variation in the control group was 6.00 compared to the vigamox group which was 2.50 as shown in figure 9.

The average percentage of endothelial hexagonal shaped cells was 55.25 in the control group preoperatively which decreased to 48.5 one month postoperatively compared to the vigamox group which was 60.71 and decreased to 54.29 as shown in figure10. Showing that there was a decrease of 6.75 in the control group and a decrease of 6.43 in the vigamox group as shown in figure 10.

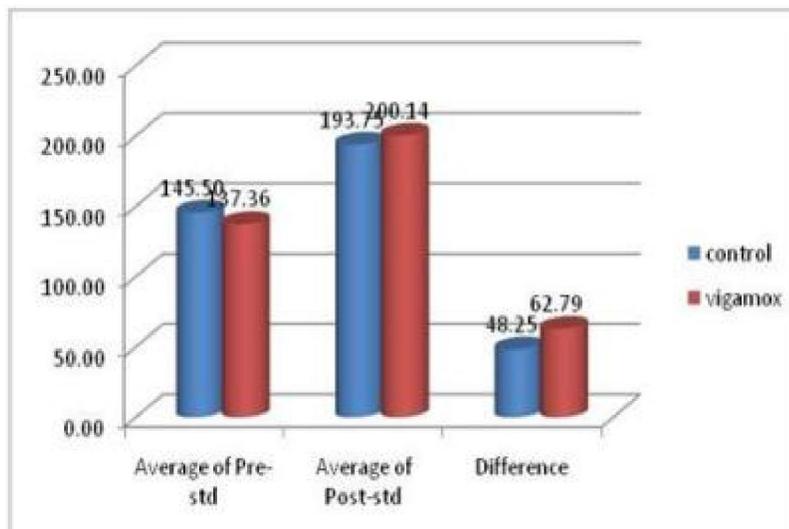


Figure 8. The difference in the average standard deviation in both groups.

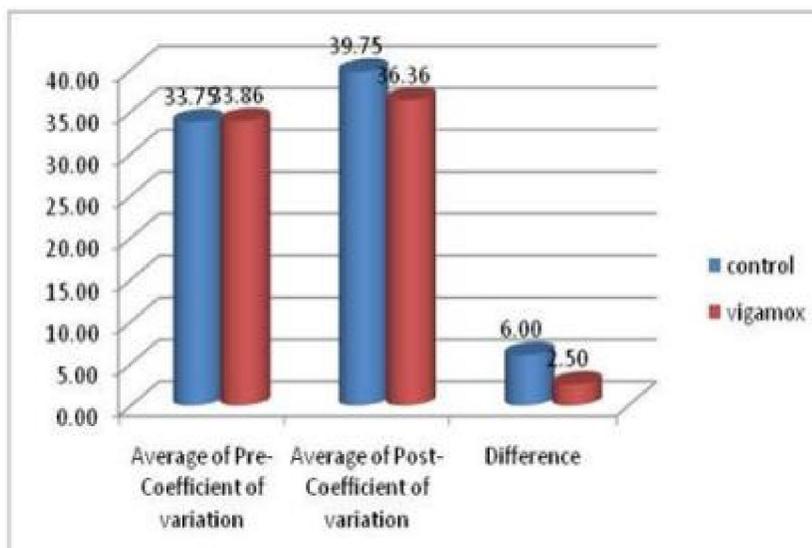


Figure 9. The average preoperative and post-operative coefficient of variation and their differences in both groups.

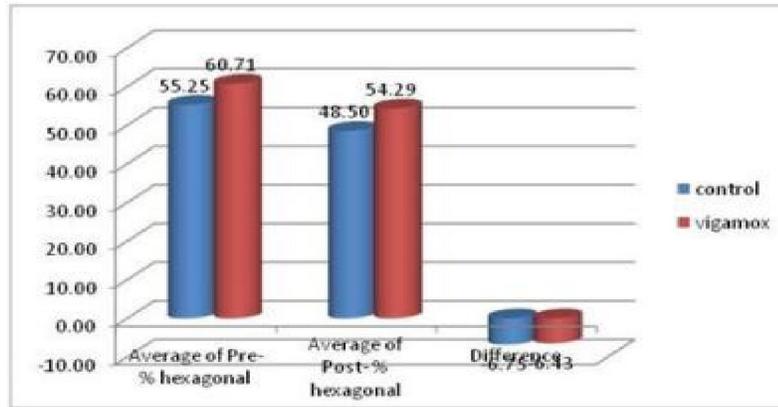


Figure 10. The percentage of endothelial hexagonal shaped cells and their difference in both groups.

The average preoperative central corneal thickness in the control group was 613 and changed to 613.75 one month postoperatively. While the average central corneal thickness in the vigamox group was 589 preoperatively and changed to 611.21 one month. The difference in the average central corneal thickness in the control group was 0.75

compared to the vigamox group which was 22.21 as shown in figure 11.

Figures 12 and 13 shows a preoperative and postoperative specular microscopy for one of the vigamox group.

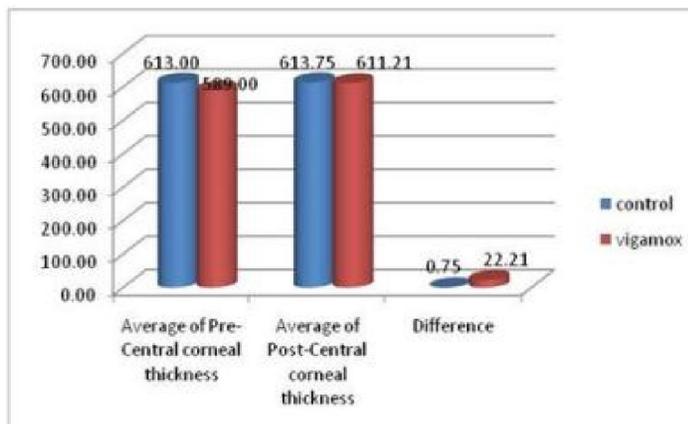


Figure 11. The average preoperative and post-operative central corneal thickness and their differences in both groups.

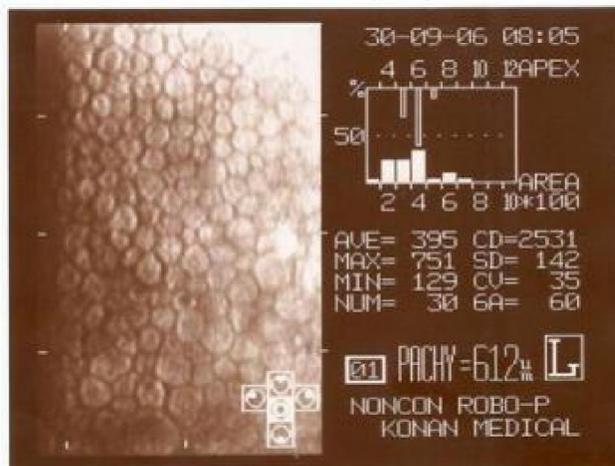
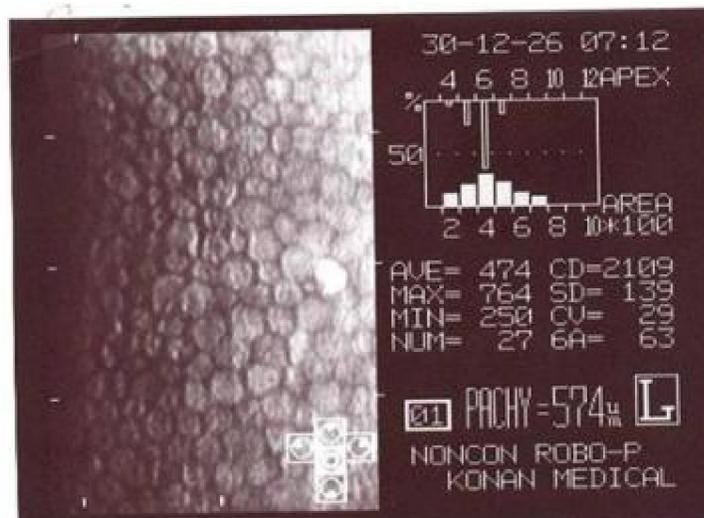


Figure 12: Preoperative Specular microscopy for a male patient in vigamox group



**Figure 13: Postoperative Specular microscopy for the same male patient in vigamox group**

#### 4. Discussion

Endophthalmitis cases after cataract surgery increased from 1994 to 2001, with a reported incidence of 2.15 per 1000 cases<sup>8</sup> this is compared to our study which was 1 eye in 60 eyes (1.667%) 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>9</sup> in a literature review of endophthalmitis prophylaxis. In addition, Isenberg et al.<sup>10</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>4,11-13</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>4</sup> thus, it seems to be a better choice for prophylactic antibiotic. The moxifloxacin injection 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, necessitate the investigation of 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.<sup>5</sup>

In 2007 **Espiritu et al.**<sup>13</sup> concerns about biocompatibility of the antibiotic by observing its effects on the cornea (endothelial cell count and pachymetry) and blood-aqueous barrier (BAB) (aqueous flare) and whether it caused inflammation in the anterior chamber (aqueous cells). Also excluded patients with corneal problems and ocular pathology other than cataract to avoid confounding the postoperative findings.

Preoperative and 1-month postoperative anterior chamber reaction, corneal endothelial cell density, and corneal thickness were assessed in 65 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 phacoemulsification. Different ophthalmologists conducted the postoperative evaluation in an observer-masked fashion. A *P*-value less than 0.05 were considered significant.<sup>14</sup>

In our study we use the same technique and dosage to be injected in 30 patients randomized in the study with a 30 control patients.

All 65 eyes completed the study. The mean age was 69.5 years  $\pm$ 9.13 (SD) (range 48 to 84 years). All eyes had a postoperative best corrected visual

acuity of 20/30 or better. All eyes had trace to C2 cells and flare anterior chamber reaction only on the first day after surgery. The mean endothelial cell count was 2491.52 cells/mm<sup>2</sup> preoperatively and 2421.58 cells/mm<sup>2</sup> postoperatively. The mean difference was 70 cells/mm<sup>2</sup>, which not statistically significant ( $P>.737$ ). The increase of 17.80 mm in postoperative pachymetry 1 month after surgery was not statistically significant ( $P>.65$ ).<sup>14</sup>

In our study 60 patients completed the study divided into 2 equal groups; the mean age was 64.2 years 7.8 years. The BCVA was 6/18 or better in 78.3 %. The mean endothelial cell count was 2516.8 cells/mm<sup>2</sup> preoperatively and 1998.8 cells/mm<sup>2</sup> postoperatively.

Thus, O'Brien found no statistical evidence of reduced endothelial cells or increased corneal thickness in their patients as early as 4 weeks postoperatively compared to preoperatively. The 3% endothelial cell loss in their 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%.<sup>14</sup> In addition, they found no proof that Vigamox causes increased BAB disturbance or secondary inflammation, which would have cause raised aqueous flare levels and raised cell levels, respectively. All eyes had 0 cells and flare at the 1-week postoperative visit. No eye lost a line of BCVA from the preoperative acuity.<sup>14</sup>

Their 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>15-18</sup> Kramann *et al.*<sup>18</sup> report no further postoperative loss of endothelial cells after 4 weeks, which suggests wound healing is complete by then. Cheng *et al.*<sup>19</sup> and Amon *et al.*<sup>20</sup> report that preoperative corneal thickness values were restored within a similar period of time.

In our study The average endothelial cell density in the control group was 2366.75cells/mm<sup>3</sup> and changed to 2083.75 cells/mm<sup>3</sup> as shown in figure 7.

While the average endothelial cell density in the vigamox group was 2533.21 cells/mm<sup>3</sup> then one month postoperatively changed to 2006.29 cells/mm<sup>3</sup> in figure 7 meaning that there was a decrease of 283 cells/mm<sup>3</sup> in the control group compared to the 526.93 cells/mm<sup>3</sup> decrease in the vigamox group. As regard the central corneal thickness. The average preoperative central corneal thickness in the control group was 613 and changed to 613.75 one month postoperatively, while the average central corneal thickness in the vigamox group was 589 preoperatively and changed to 611.21 one month as shown in figure11.

The difference in the average central corneal thickness in the control group was 0.75 compared to the vigamox group which was 22.21as shown in figure11.

The average preoperative central corneal thickness in the control group was 613 and changed to 613.75 one month postoperatively as shown in figure11.

Although, they found no proof that Vigamox causes increased BAB disturbance or secondary inflammation, which would have cause raised aqueous flare levels and raised cell levels, respectively. All eyes had 0 cells and flare at the 1-week postoperative visit.

But in our study, Slit Lamp Examination revealed 1-2+ cell and flare for control group and 3-4+ cells and flare for Vigamox group in the first visit. Corneal edema proportional to ultrasound time for control group but slightly more in Vigamox group. Eight patients showed moderate corneal edema and two cases showed severe corneal edema.

Improvement in all patients with decrease of corneal edema and also slight decrease in cells and flare recorded at day 3 postoperatively. By the first week, Little corneal edema and trace to 0/1+ cell and flare for control group and 1/2+ cell and flare for Vigamox group which disappeared completely by the second week.

In their study No eye lost a line of BCVA from the preoperative acuity.<sup>14</sup>

Similarly, in our study No eye lost a line of BCVA from the preoperative acuity except one case from our control group showed increase in flare and cells with hypopyon and signs of endophthalmitis with a final BCVA of 3/60.

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. They injected 0.1 mL 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>21</sup> Granting that they 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 0.525 mL, or 952 mg/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 their cases was

at least 300 times the median MICs of endophthalmitis-causing organisms.

Development of resistant strains through mutation with the prophylactic use of antimicrobials is another parameter by which to evaluate antibacterial potency. This drug level, called the mutant prevention concentration (MPC), addresses the concern that frequent, suboptimal use of antibiotics increases the chances for and hastens the appearance of resistant mutants. Knowing, and more important achieving, concentrations above these levels more or less ensures prevention of such strains. The MPC of fluoroquinolones is typically 8 to 10 times their MIC.<sup>22,23</sup> Calculations show that the moxifloxacin concentrations initially achieved in their 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 a dearth of data in the literature on the bioavailability of antibiotics after intraocular administration in humans.<sup>13,24-27</sup> 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.<sup>17</sup> The investigators, however, instilled the antibiotic (cefuroxime) in a nondistended 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.<sup>13,24-27</sup> 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.<sup>25,28</sup>

Also to determine whether Vigamox (moxifloxacin 0.5% ophthalmic solution) can be safely injected intracamerally to prevent *Staphylococcus aureus* endophthalmitis in a rabbit model. Kowalski *et al.* in 2005<sup>29</sup> studied the safety and bactericidal effectiveness of Vigamox which were evaluated in three stages using 189 New Zealand White rabbits. (Stage 1) The toxicity of two intravitreal doses of Vigamox (moxifloxacin 500, 250

microg) was compared with vancomycin (1 mg) and saline. (Stage 2) A reproducible rabbit model of *Staphylococcus aureus* endophthalmitis was established. (Stage 3) The bactericidal effect of intracameral Vigamox (moxifloxacin 500, 250, 125, 50 µg) was compared with vancomycin (1 mg) and saline. Intracameral antibiotic therapy commenced immediately after *Staphylococcus aureus* intravitreal challenge (5000 cfu). Toxicity was evaluated by masked clinical examination using a slit-lamp, an indirect ophthalmoscope, and corneal-ultrasound pachymetry. The clinical examination included the exterior eye, cornea, anterior chamber, vitreous, and retina. The presentations were graded on a severity scale of 0, 0.5, 1, 2, and 3. The bactericidal efficacy was determined using intracameral colony counts.<sup>29</sup>

In the toxicity studies without bacterial challenge, the clinical scores of rabbits injected intracamerally with Vigamox were statistically equivalent to rabbits given intracameral vancomycin or saline. In the efficacy studies, eyes treated intravitreally with Vigamox, at all doses, or vancomycin were negative for *Staphylococcus aureus* and non-treated controls remained culture-positive.

Kowalski *et al.*<sup>29</sup> concluded that Vigamox appears to be nontoxic for intracameral injection and effective in preventing experimental endophthalmitis in the rabbit model.

In our study, we concentrated on safety not efficacy so we didn't measure intraocular concentration or the bioavailability of the drug.

Gao *et al.*<sup>30</sup> concluded that: Intravitreal moxifloxacin, up to 100 microg/mL in mice or 150 microg/mL in rabbits, caused no ERG or retinal histologic abnormality. These results indicate that moxifloxacin is a safe intravitreal antibiotic in mouse and rabbit animal models. If proven safe and efficacious by further study in humans, intravitreal injection of moxifloxacin could be considered as an alternative to currently used antibiotics in selected patients with resistance or allergy to the more traditional antibiotics.<sup>30</sup>

In our study only intracameral injection of moxifloxacin was studied but not intravitreal injection.

In 2008 Lane *et al.*<sup>31</sup> evaluation came to the conclusion that there was no increased safety risk associated with a 250 µg/0.050 mL intracameral injection of moxifloxacin, which appears to be safe in the prophylaxis of endophthalmitis after cataract surgery.

In our study we injected 0.1cc of Moxifloxacin 0.5% (5 mg/mL), taken from newly opened bottle of vigamox eye drop which showed significant affection of the endothelial cells compared with the control group even though resolution of all

flare and cells as well as corneal edema occurred by the third week of follow up.

Kim *et al.*<sup>32</sup> concluded that Intracameral injection of antibiotics (cefazolin 1000 microg/0.1 mL, levofloxacin 500 microg/0.1 mL, moxifloxacin 500 microg/0.1 mL) did not show significant toxicity on the endothelial cells compared with the control group. Intracameral injection of one of these antibiotics appears to be safe for surgical prophylaxis.<sup>32</sup>

In 2010 Kernt *et al.*<sup>27</sup> investigated the safety of Vigamox for intracameral application in a cell-culture model. No corneal endothelial toxicity could be detected after 30 days of treatment with moxifloxacin 500 µg/ml. Primary RPEs, TMCs, LECs, and CECs showed adverse effects on proliferation and viability only at concentrations higher than 150 µg/ml moxifloxacin. After preincubation with TNF- $\alpha$ , LPS, and IL-6 for 24 hrs and subsequent treatment with moxifloxacin at concentrations of 10-150 microg/ml for 24 hrs, no significant decrease in proliferation or viability was observed. H<sub>2</sub>O<sub>2</sub> exposure did not increase cellular toxicity. Thus they concluded that Vigamox did not show significant toxicity on primary RPEs, TMCs, LECs, CECs, or human corneal endothelium at concentrations up to 150 microg/ml. The MIC<sub>90</sub> of moxifloxacin for pathogens commonly encountered in endophthalmitis is known to be in the range of 0.25-2.5 µg/ml. Therefore, intracameral use of Vigamox at concentrations up to 150 microg/ml may be safe and effective for preventing endophthalmitis after intraocular surgery.<sup>27</sup>

Even in routine uncomplicated phacoemulsification, vision loss can occur due to postoperative cystoid macular edema (CME).<sup>33</sup> It is thought to be caused by intraocular inflammation causing accumulation of intraretinal fluid.

Wittmann *et al.*<sup>34</sup> did a prospective study, in which subjects were randomized to receive either perioperative ketorolac 0.4% (3 days prior to surgery, as well as 4 doses every 15 minutes for 1 hour before surgery) plus postoperative prednisolone 1% or prednisolone alone. A total of 546 patients were enrolled and randomized to either the ketorolac/steroid group (n = 268) or steroid-only group (n = 278). Based on biomicroscopy, 5 cases of CME were identified in the steroid group, whereas none were seen in the ketorolac/steroid group. When using optical coherence tomography (OCT) imaging, the incidence increased to 6 for the steroid-alone group; the combination treatment group had no CME cases identified by OCT.

This demonstrates that the addition of topical ketorolac prevents postoperative CME in low-risk cataract patients. Although the incidence of CME

was low without pretreatment with ketorolac (6/278 or 2%), the vision loss from CME can be significant. The authors<sup>34</sup> also noted that the cost to treat CME among Medicare patients was \$3298; therefore, this addition to surgery may be quite cost effective.<sup>34</sup> In our study, only one case showed CME.

## 5. Conclusion

Intracameral 0.1 ml of 0.5% moxifloxacin (Vigamox, Alcon) was found to be safe for the visual rehabilitation and corneal endothelium. Use of Intracameral moxifloxacin can be a beneficial adjunct to topical dosing for surgical prophylaxis. Further, studies to prove its effectiveness in preventing endophthalmitis are required.

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