

Efficacy of intraoperative vancomycin in irrigating solutions on aqueous contamination during phacoemulsification

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Purpose: To study the efficacy of adding vancomycin in irrigating solutions, in comparison to topical antibiotic given preoperatively for a day, during phacoemulsification, in reducing the anterior chamber (AC) contamination.

Settings and Design: This was a prospective, interventional, hospital-based study.

Materials and Methods: This was a study involving 400 eyes of 400 patients, undergoing routine phacoemulsification between January 2004 and June 2006. The patients were non-randomly assigned to two groups: Group 1 included 180 patients, who received topical ciprofloxacin eye-drops (four-hourly) for a day preoperatively and Group 2 included 220 patients, who underwent phacoemulsification with vancomycin (20 µg/ml) in the irrigating solution. Anterior chamber aspirate obtained at the end of the surgery was sent for microbial workup. The number of positive cultures in both the groups was determined.

Statistical analysis: This was performed using Chi-square test.

Results: Aqueous samples showed microbial growth in 38 (21.1%) out of 180 eyes in Group 1 and in 17 (7.7%) out of 220 eyes in Group 2 ($P = 0.001$). *Coagulase-negative staphylococcus* was the most common organism in both the groups. Aqueous samples from four eyes in group 1 showed multiple organisms, while none of the sample from group 2 showed more than one organism. None of the eyes in either group showed fungal contamination. One patient in Group 1 developed endophthalmitis, and the causative organism was *Alcaligenes faecalis*. All patients were followed up for a minimum of six months (range: 6 to 14 months and mean: 9.3 months).

Conclusion: Addition of vancomycin in irrigating solutions is more efficacious in reducing AC contamination in comparison to topical antibiotic administered a day preoperatively.

Key words: Anterior chamber contamination, intraoperative vancomycin, phacoemulsification, preoperative antibiotics, prophylaxis and endophthalmitis

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Postoperative endophthalmitis is a rare but devastating complication of cataract surgery and remains one of the most feared problems following intraocular surgeries. Although the frequency of endophthalmitis has declined over the years, most studies still report an incidence between 0.07% and 0.1%.¹⁻⁴ Some recently concluded studies have shown that intracameral injections of cefuroxime administered at the time of surgery⁵ or the use of subconjunctival antibiotics⁶ significantly reduces the risk of developing endophthalmitis after cataract surgery. However, use of intracameral cefuroxime has been associated with toxic anterior segment syndrome,⁷ anaphylactic reactions^{8,9} and increased incidence of cystoid macular edema,¹⁰ thus benefit should be weighed against side-effects.

Topical antibiotics can be used preoperatively for one

to three days to reduce the load of microorganisms in the conjunctival flora, thus minimizing the anterior chamber (AC) contamination.^{11,12} Antibiotics are being added to the irrigating solution while performing cataract surgery, as a prophylaxis against persistence of the organisms entering in the AC. A recently published study had shown that antibiotics (vancomycin and gentamicin) in irrigating fluids can be used to decrease AC contamination.¹³

The reduction in intraocular contamination during phacoemulsification is essential to prevent endophthalmitis.¹⁴⁻¹⁶ The aim of this prospective study was to compare the efficacy in reducing the AC contamination between preoperative topical 0.3% ciprofloxacin eye-drops and addition of vancomycin in a concentration of 20 µg/ml in the irrigating solution by comparing the number of positive postoperative intraocular cultures in both groups.

Materials and Methods

Patients undergoing routine phacoemulsification cataract surgery between January 2004 and June 2006, more than 25 years of age and ready to give written informed consent and not falling in the exclusion criteria were recruited in this

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study. Ethical committee clearance was obtained. The exclusion criteria were:

- The patient having undergone prior intraocular surgery,
- The patient having received any topical or systemic antibiotics within 10 days prior to the enrollment into this study,
- Any source of local or systemic infection,
- Evidence of any systemic disease,
- The patient who required additional procedure along with phacoemulsification,
- The patient not ready to give consent for enrollment into the study.

The patients were non-randomly assigned to two groups: 1 and 2. Patients enrolled in the study during the initial 15 months of the study were included in Group 1, while the patients getting enrolled in the later 15 months of the study were enrolled in Group 2. Group 1 included patients who received topical 0.3% ciprofloxacin (Ciplox-0.3%, Cipla Ltd.) eye-drops (four-hourly) for a day preoperatively but did not receive vancomycin (VanSafe-CP, VHB Life sciences Inc.) in the irrigating solution during cataract surgery, while Group 2 included patients who received vancomycin (20 µg/ml) in the irrigating solution during cataract surgery but did not receive topical antibiotics preoperatively.

One hour preoperatively pupils were dilated using 1% cyclopentolate (Cyclopet, Sun Pharmaceutical Ltd.) and 10% phenylephrine (Drosyn, FDC Ltd.) eye-drops. Flurbiprofen 0.03% (Flur, Allergan India Pvt Ltd.) eye-drops were used for sustained pupil dilatation. The eyes were anesthetized by peribulbar block, using 6 ml mixture containing equal parts of 0.5% bupivacaine [Bupivacaine hydrochloride, SPM drugs Ltd.] and 2% lignocaine (Loxicard, Neon Laboratories Ltd.) with 375 IU/ml of hyaluronidase (Omnidase, Sunways India Pvt Ltd.) The eyelids, nose, cheek, eyebrow, and forehead were scrubbed with 5% povidone-iodine (Aptidine-5, Appasamy Ocular Devices Pvt Ltd.) for 3 min and with 70% alcohol for another minute. Two drops of 5% povidone-iodine eye-drops were instilled in the conjunctival sac 5 min before surgery. A sterile drape with an adhesive foil was used to exteriorize the eyelashes. All surgeries were performed by the same surgeon (RS).

In both the groups, phacoemulsification was performed through a 3.2-mm self-sealing superior scleral incision. Sterile compound sodium lactate (Mount Mettur pharmaceuticals) with epinephrine (Tidrenelene, Tamman Titoe Pharma Pvt Ltd.) 1:10,000 dilution (for infusion) and hydroxypropyl methylcellulose (Appavisc PFS, Appasamy Ocular Devices Pvt Ltd.) as viscoelastic material were used during the surgery. However, in Group 2 patients, vancomycin (20 µg/ml) was added in the irrigating solution. After the surgery incision was enlarged, a 5.25 mm, single-piece, polymethyl methacrylate posterior chamber intraocular lens (Appalens, Appasamy Ocular Devices Pvt Ltd.) was implanted in the bag. At the end of the surgery, after the removal of all viscoelastic material, 0.2 ml of anterior chamber fluid was aspirated through the side port incision with a 27-gauge cannula mounted on a tuberculin syringe for the microbiological study. Only one microbiologist was involved in the study for the purpose of analysis.

The aspirates collected from both the groups were treated identically. They were inoculated onto blood agar, chocolate

agar, thioglycolate broth and Sabouraud dextrose agar. The chocolate agar was incubated at 37°C in 5% carbon dioxide for five days, and then incubated at 30°C without carbon dioxide for an additional 10 days to study the fastidious organisms before considering it to be negative. The thioglycolate broth was incubated at 37°C aerobically for three weeks and sub-cultured onto chocolate agar in 5% carbon dioxide and blood agar anaerobically. Sabouraud dextrose agar was incubated aerobically at 37°C for 28 days before declaring it to be negative. Colony characteristics and cell morphology were examined under the microscope. The necessary biochemical tests were conducted and the organisms were identified using standard procedures.¹⁷ Antibiotic sensitivity was determined using broth dilution method.¹⁸ Statistical analysis was carried out using the Chi-square test.

Results

A total of 402 samples were taken from 402 eyes. Two eyes were excluded from the study, as the aqueous humor was inadequately collected and was realized later. Four hundred eyes (of 400 patients) were enrolled in the study, of which 180 belonged to Group 1 and 220 eyes belonged to Group 2 respectively. The difference in the number of patients between the two groups was due to the specific enrollment method adopted. There were 240 men and 160 women. Patients were in the age group of 30 to 78 years (average 57 years). The right eye was operated in 212 patients (53%) and the left eye in 188 patients (47%).

Bacteria were cultured from AC aspirates in 38 out of 180 eyes (21.1%) in Group 1 and 17 out of 220 eyes (7.7%) in Group 2 ($P = 0.001$). Multiple organisms were identified in four eyes (2.2%) in Group 1 while none of the eyes in Group 2 showed multiple organisms. *Coagulase-negative staphylococcus* was the most common organism isolated in both the groups. Eight different bacteria were cultured in Group 1 and five in Group 2. None of the eyes showed fungal contamination. The strains of bacteria cultured from the AC aspirates are shown in Table 1. Most of the isolated bacteria were sensitive to vancomycin, with minimum inhibitory concentrations between 0.5 and 2.0 µg/ml.

None of the eyes had any intraoperative complication. However, one patient in Group 1 developed endophthalmitis postoperatively and the organism cultured from AC initially during surgery as well as from intra-vitreous aspirate later showed *Alcaligenes faecalis*. This patient responded to intravitreal antibiotics, however, the final visual outcome was poor due to consecutive optic atrophy. All patients were followed up for a minimum of six months, with a range of 6 to 14 months (mean: 9.3 months).

Discussion

Despite technical improvements in cataract surgery, endophthalmitis still remains the most dreaded complication of intraocular surgery. Gram-positive organisms are responsible for acute postoperative endophthalmitis in more than 90% of cases. More than half of these are due to *Staphylococcus epidermidis* infections, which may be due to its abundance in the conjunctival flora.¹⁹ Conjunctival flora organisms are responsible for postoperative endophthalmitis in the majority of cases.²⁰ Studies of DNA have shown that in *Staphylococcus*

Table 1: Results of anterior chamber cultures (n = 400)

Organism	Group-I (n = 180)		Group-II (n = 220)	
	Number	% out of total number of organisms	Number	% out of total number of organisms
Coagulase-negative <i>Staphylococcus</i>	24	57.14	11	64.7
<i>Propionibacterium acnes</i>	2	4.7	-	-
<i>Staphylococcus aureus</i>	4	9.4	2	11.7
<i>Acinetobacter Iwoffii</i>	4	9.4	1	5.8
<i>Enterobacter species</i>	2	4.7	2	11.7
<i>Acinetobacter anitratus</i>	2	4.7	-	-
<i>Diphtheroids</i>	3	7.1	1	5.8
<i>Alcaligenes faecalis</i>	1	2.4	-	-
Total	42	100.0	17	100.0

Note: In Group 1, four patients showed two organisms

epidermidis endophthalmitis, the most common source of infection is the patient's own flora.²⁰

Ciprofloxacin and vancomycin are efficient against the gram-positive organisms. Intraocular vancomycin has been shown to be safe in doses up to 20 mg/l of vancomycin in irrigating solution.¹⁶ The best choice for antimicrobial treatment of gram-negative organisms is controversial. Aminoglycosides have traditionally been recommended for gram-negative coverage. Several clinical and laboratory reports have shown that intravitreal aminoglycosides are toxic to the retina and retinal pigment epithelium at doses close to the therapeutic level and are thus avoided as a routine antibiotic in irrigating fluids.²¹

A study to evaluate the difference in the frequency of endophthalmitis between two prophylactic regimens would require thousands of cases to be statistically significant. As a result, conclusions about efficacy in the prophylaxis of endophthalmitis have frequently been based on the effect of different regimen on conjunctival flora or intraocular cultures obtained at the end of the surgery.¹³ Pospisil *et al.*, found two patients with postoperative endophthalmitis in a study of 15 eyes with positive intraocular cultures but no endophthalmitis in any of the 47 eyes with negative culture results.²²

The absence of clinical ocular infection in patients with positive culture at the end of surgery attests to the small size of inoculum and the ability of the AC to clear small bacterial loads.²³ In an attempt to reduce the bacterial load from the conjunctival flora, preoperative topical antibiotic is being practiced widely but some studies have shown it to be of doubtful benefit clinically.²⁴ Ta *et al.*, showed no significant difference in AC contamination between preoperative antibiotics of three days or one hour.²⁴

In the present study, vancomycin was selected because of its activity against pathogens that commonly cause endophthalmitis and its safety in the form of prophylaxis.^{13,21} The appropriate antibiotic concentration and the time necessary to effectively eliminate microorganisms after surgery are unknown. The half-life of vancomycin in the AC has been shown to be about two hours.¹¹ Robert *et al.*, reported that the solutions in the AC at the end of surgery may be present for six to eight hours, but no data are available about the duration of effectiveness of antibiotic concentrations in the AC after being used in irrigating solutions²⁵ though a contact period of two

hours is recommended for the antibiotics to sterilize the AC.²⁶ In our study, the contact period of organisms with vancomycin was less than two hours in Group 2 patients, which might be the reason for the aqueous aspirate showing growth of organisms, despite some of them being sensitive to vancomycin.

The major limitations of this study are the small sample size in both the groups, non-randomization in the selection of the sample size, unequal sample size in the two groups. The patients in the two groups were not enrolled simultaneously, but there was a gap of 15 months between the initiation of selection of patients in the two groups. Though this study aims to prove the use of vancomycin in irrigating solution as a prophylactic method for the prevention of endophthalmitis, there is no direct relationship between AC contamination and the endophthalmitis.^{13,20,24} Also, routine use of antibiotic may lead to the emergence of resistance against vancomycin. The US centers for Disease Control and Prevention have cautioned against the generalized use of powerful antibiotics such as vancomycin because of the emergence of vancomycin-resistant strains of *coagulase-negative staphylococcus* and *enterococcus*.²⁷

We conclude that the addition of vancomycin to the irrigation solutions during uncomplicated phacoemulsification with posterior chamber IOL implantation reduces the frequency of positive intraocular cultures at the end of surgery as compared to the ciprofloxacin eye drops used preoperatively. Additional data about the selection of most appropriate antibiotic or antibiotic combinations, dosage, safety and efficacy of this form of treatment are needed before this prophylactic technique can be routinely used during cataract surgery.

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