

The effect of intraoperative antibiotics in irrigating solutions on aqueous humor contamination and endophthalmitis after phacoemulsification surgery

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PURPOSE. *To determine the efficacy of intraoperative antibiotic use in irrigating solutions on aqueous humor contamination during phacoemulsification surgery and to evaluate the corresponding risk of postoperative endophthalmitis.*

METHODS. *644 eyes of 640 patients who underwent phacoemulsification surgery with foldable intraocular lens (IOL) implantation were included in this study. Preoperative conjunctival smears were taken and eyes were allocated to receive irrigating infusion fluid containing either balanced salt solution (BSS)-only (group 1; 322 eyes) or BSS with antibiotics (vancomycin and gentamycin) during surgery (group 2; 322 eyes). Bacterial contamination rates of aqueous humor samples taken in the beginning and at the end of operation were compared. Predictive factors for the development of postoperative endophthalmitis were determined by clinical and microbiologic analyses.*

RESULTS. *The rates of culture-positivity were similar between group 1 and group 2 for both preoperative conjunctival smears and aqueous samples ($p > 0.05$). Aqueous samples taken at the end of operation were found to be contaminated in 68 (21.1%) eyes in group 1 and 22 (6.8%) eyes in group 2, and the difference was significant ($p = 0.0001$; OR = 3.65 (2.1-6.0)). Capsular rupture was associated with higher rate of contamination in both groups ($p = 0.0001$; OR = 7.7 and $p = 0.0001$; OR = 8.1). Two eyes in the BSS-only group developed postoperative endophthalmitis and these cases had posterior capsular rupture during the surgery and culture-positivity for staphylococcus epidermidis throughout the study.*

CONCLUSIONS. *Intraoperative antibiotic irrigation decreases aqueous humor contamination during phacoemulsification. Further studies are warranted to determine the interrelationship between aqueous humor contamination and endophthalmitis in eyes with posterior capsular rupture. (Eur J Ophthalmol 2003; 13: 773-8)*

KEY WORDS. *Endophthalmitis, Intraocular antibiotics, Microbiology, Phacoemulsification*

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INTRODUCTION

The incidence of postoperative endophthalmitis (PE), a serious complication of cataract surgery, has declined over the past 30 years because of improved surgical techniques, antiseptic measures, and the use of antibiotics before, during, and after surgery (1-3). Most organisms causing postoperative endophthalmitis are believed to originate from the external ocular bacterial flora of the patient (2,4,5). The value of preoperative topical antibiotic therapy is still uncertain because it does not eradicate all the microorganisms on the external ocular surface. However, such therapy may reduce bacterial growth to a sub-threshold level, thus reducing the incidence of postoperative endophthalmitis (3,6-9). During surgery, microorganisms may enter into the eye through air in the operating room, irrigating solutions, instruments, or intraocular lenses (IOLs) (7,10-12). Although the incidence of postoperative endophthalmitis is very low (around 0.1%) (13), contamination of the anterior chamber fluids at the end of cataract surgery has been reported to be as high as 28% (14).

Irrigating infusion fluid containing antibiotics is known to be effective in decreasing aqueous humor contamination (15-18). However, contradictory reports are present in the literature and the value of intraoperative antibiotics for the elimination of bacterial contamination of the aqueous humor and the development of postoperative endophthalmitis is still unclear (19,20). Therefore, the present study aimed to determine the significance of intraoperative antibiotic use on the aqueous humor contamination and on the development of PE in eyes with phacoemulsification surgery.

METHODS

Six hundred forty four eyes of 640 patients who underwent phacoemulsification surgery at Gülhane Military Medical Academy and Medical School Hospital between May 2000 and June 2002 were included in this study. Informed consent was obtained in all cases. Patients were randomly allocated to irrigating infusion fluid containing either balanced salt solution (BSS)-only (group 1; 322 eyes of 320 patients) or BSS with antibiotics (20 mg/ml vancomycin and 8 mg/ml gentamicin) (group 2; 322 eyes of 320 patients), ac-

ording to the scheduled day of surgery, which was performed one after another. (1:1). Patients with previous history of immunosuppressive treatment, diabetes mellitus, ocular surgery and recent infection or inflammation were all excluded from the study. Phacoemulsification was performed with a standard 3.2-mm clear corneal incision, circular capsulotomy, and stop-chop technique followed by foldable hydrophobic acrylic IOL (Acrysof, Alcon) implantation using forceps. The operation was ended with no suture, subconjunctival antibiotic or steroid injection. The eyes in which the surgical procedure was modified by the surgeon's discretion, such as suturing and use of subconjunctival antibiotics were not included in the study. All patients received a one-day course of topical ofloxacin (0.3%) and diclofenac sodium (1mg/ml) 4 times a day preoperatively. A preoperative conjunctival smear was obtained in all cases from the inferior cul-de-sac with a sterile cotton wool swab just before povidone-iodine instillation. It was first immersed in thioglycolate broth, plated onto blood and chocolate agar. The chocolate and horse blood agar plates were incubated 48 h in carbon dioxide 5% at 37°C and examined at 24 hours. The thioglycolate broth tubes were incubated at 37°C for 2 weeks. In order to confirm the presence of aerobic or anaerobic bacteria, the growth was also cultured in both chocolate and fastidious anaerobic agar plates. The identification of microorganisms and the profile of antibiotic sensitivity were determined using standard methods (21,22). Aqueous humor aspirates were taken entering the anterior chamber just before viscoelastic injection (sample 1) and ending the operation just before BSS injection into wound edges (sample 2), avoiding vascular contact or damage to the intraocular tissues. Postoperatively, the eyes were treated with ofloxacin (0.3%), dexamethasone (1mg/ml) and indomethasine (0.1%) drops for a four-week tapering dose. Patients were discharged from the hospital on the first day after surgery and examined on days 2, 5, 10, 15, 30 and 45. Postoperative endophthalmitis was defined as the presence of hypopyon, clouding of the anterior chamber, or vitreous, which is severe enough to obscure the visualization of the second-order retinal arterioles within 6 weeks after the surgery (23,24).

Qualitative and quantitative analyses of microbiologic spectrum in preoperative and intraoperative cultures were performed in all eyes. In the case of post-

operative endophthalmitis, culture results were obtained from the aqueous humor and vitreous samples. The association of clinical and microbiologic factors with bacterial contamination of aqueous humor and the development of postoperative endophthalmitis was sought.

Statistics. Chi-squared or Fischer's exact test was used as indicated. A p-value below 0.05 was considered to be significant. Statistical analysis was performed with Statistical Package for the Social Sciences for Windows (Version 10.0, SPSS Inc., Chicago, IL, USA).

RESULTS

All patients had senile cataract and the mean age was 64.2 ± 14.3 (range 43-87) years and 61.2 ± 14.2 (range 40-81) years for group 1 and group 2 respectively ($p = 0.47$). The mean operation time was 22.2 ± 8.8 (range 10-45) minutes and 20.4 ± 7.8 (range 10-40) minutes respectively ($p = 0.28$). Of 644 preoperative conjunctival smears, 188 (58.3%) of 322 eyes showed positive cultures in group 1, and 184 (57.1%) of 322 in group 2 ($p = 0.75$). The most frequent cultured organism was coagulase-negative staphylococci com-

prising 120 of 188 (63.8%) eyes in group 1 and 118 of 184 (64.1%) eyes in group 2 ($p = 0.95$) which was sensitive to ofloxacin (0.3%), in 105 out of 120 samples (87.5%). The number of eyes with mixed microorganisms was similar between the groups (in each, $n = 12$ eyes). Contamination rates of aqueous humor aspirates in group 1 ($n = 13$; 4.0%) and group 2 ($n = 15$; 4.6%) at the beginning of the operation (sample 1) were found to be similar ($p = 0.65$). However, aqueous humor aspirates in sample 2 were contaminated in 68 (21.1%) of 322 eyes in group 1 and in 22 (6.8%) of 322 eyes in group 2 ($p = 0.0001$, OR = 3.65 (2.1-6.0)) (Tab. I). From 47 eyes in which coagulase-negative staphylococci was cultured from aqueous humor samples, 40 eyes (85.1%) were found to be sensitive to that topically applied antibiotic. The coagulase-negative microorganism cultured from eyes with endophthalmitis was also sensitive to that antibiotic in all samples. Two eyes with culture-proven endophthalmitis were complicated by posterior capsular rupture during the operation. The number of intraoperative posterior capsular rupture between group 1 ($n = 16$; 4.9%) and group 2 ($n = 12$; 3.7%) was similar ($p = 0.44$). Aqueous humor sample was found to be contaminated in 14 of 28 (50%) eyes with posterior capsular rupture, and 76 of 616 (12.3%) eyes

TABLE I - MICROORGANISMS ISOLATED FROM THE PREOPERATIVE CONJUNCTIVAL SMEARS AND INTRA-OPERATIVE AQUEOUS HUMOR ASPIRATES

Microorganisms	Conjunctival Smear		Aqueous Humor Sample 1		Aqueous Humor Sample 2	
	Group 1 (%)	Group 2 (%)	Group 1 (%)	Group 2 (%)	Group 1 (%)	Group 2 (%)
Coagulase(-)Staphylococcus	120(63.8)	118(64.1)	5(38.4)	6(40)	28(41.2)	8(36.4)
Staphylococcus aureus	28(14.9)	26(14.1)	-	3(20)	8(11.8)	4(18.2)
Corynebacteria	-	-	2(15.3)	4(26)	10(14.7)	6(27.3)
Streptococcus epidermidis	-	-	1(7.6)	2(13.3)	6(8.8)	2(9.1)
Pseudomonas aeruginosa	-	-	2(15.3)	-	4(5.9)	-
Mixed (Pseudomonas, Klebsiella)	-	-	1(7.6)	-	8(11.8)	2(9.1)
Bacillus species	-	-	2(15.3)	-	4(5.9)	-
Streptococcus pneumoniae	8(4.3)	6(3.3)	-	-	-	-
Proteus mirabilis	6(3.2)	6(3.3)	-	-	-	-
Enterobacter cloacae	14(7.4)	16(8.7)	-	-	-	-
Mixed (Staph.aureus, Enterobac.)	12(6.4)	12(6.5)	-	-	-	-
Eyes	188(58.3)	184(57.1)	13(4.0)	15(4.6)	68(21.1)	22(6.8)*

* $p = 0.0001$

with intact capsule ($p = 0.0001$; OR = 7.1 (3.2-15.4)). The association of posterior capsular rupture to higher contamination rate was evident in both groups. Aqueous humor aspirate was contaminated in 10 of 16 eyes (62.5%) with capsular rupture in group 1 ($p = 0.0001$; OR = 7.7 (2.7-32.3)) and 4 of 12 eyes (33.3%) with capsular rupture in group 2 ($p = 0.0001$; OR = 8.1 (2.2-29.5)). The mean operation time of 28.8 ± 6.4 minutes in eyes with capsular rupture were significantly higher than that of 18.2 ± 7.0 minutes in eyes with intact capsule ($p = 0.001$). Postoperative endophthalmitis was noted in 2 eyes of 2 patients in group 1 (BSS-only group). The aqueous and vitreous specimens were obtained 2 and 5 days after the surgery and were found to be positive for coagulase-negative staphylococci. Preoperative and intraoperative cultures for both sample 1 and sample 2 in these eyes were also positive for the same microorganism.

DISCUSSION

There is evidence that surface flora routinely gain entry into the anterior chamber during cataract surgery (14). In a prospective study of 230 consecutive patients, Egger et al demonstrated that phacoemulsification was superior to ECCE with its lower aqueous humor contamination (25). On the other hand, in a prospective study of 700 patients, Mistlberger et al reported that rate of aqueous humor contamination was similar between ECCE and phacoemulsification surgeries and preoperative antibiotic treatment had no influence on the rates of intraoperative aqueous humor contamination (26).

As was reported previously, coagulase-negative staphylococcus was the most common isolated microorganism (64%) from the conjunctiva in this study (26-28). Povidone-iodine has been reported to be of primary importance in providing preoperative prophylaxis (13). We also instilled preoperative povidone-iodine in all cases. We clearly demonstrated that the rate of aqueous humor contamination was significantly decreased when the irrigating solution contained antibiotics throughout the surgery. The microbiologic spectrum in aqueous humor samples was also similar to previous reports and coagulase-negative staphylococcus was the most common microorganism in either group (26, 27, 28). It is important to note that many species

isolated from the aqueous humor were virulent in both groups. Only 2 eyes (3.10%) developed postoperative endophthalmitis. We think that this exceptionally high rate of endophthalmitis can be explained by the lack of sufficient material to reach a final conclusion, if we consider that the cumulative rate of postoperative endophthalmitis (in a 5-year review of all cases with cataract surgery) at our institute is 0.109%. Both eyes infected by coagulase-negative staphylococcus (*Staphylococcus epidermidis*), which was sensitive to vancomycin and ofloxacin (0.3%) (Tab. I). It is noteworthy that this microorganism was also cultured in conjunctival smear and aqueous samples of both eyes. It was reported that half-life of intraoperative antibiotics was less than 2 hours and was an ineffective prophylaxis for postoperative endophthalmitis (29). However, Mendivil and Mendivil (17) reported that a lower rate of contamination was obtained in eyes irrigated with an intraoperative antibiotic (vancomycin). Indeed, it has been reported that the use of intraoperative antibiotics reduces bacterial adherence to IOLs (30). We thought that the lower rate of aqueous contamination in group 2 was due probably to the inhibition of colonization by intraoperative antibiotics.

However, potential retinal toxicity from intraocular antibiotics should be taken into account when the decision is being made to add antibiotics to the infusion fluid. Although we tried to exclude the bias for the surgical technique, and eliminate IOL contamination during its insertion, the amount of bacterial loading and immunologic status of the eye might have been involved in the difference of aqueous humor contamination rates between the groups. Since we did not perform successive culturing from conjunctival smears and aqueous humor samples postoperatively, we were not certain about the role of postoperative topical antibiotics for prophylaxis of endophthalmitis. The microorganism, coagulase-negative staphylococcus cultured preoperatively and postoperatively was found to be sensitive to topical ofloxacin (0.3%) in 87.5% eyes (not shown in the table). This underscores the presence or development of resistance to this antibiotic in our population. Likewise, this subject is still open to debate for vancomycin. The selection of vancomycin was based on the etiological spectrum of our previous cases with endophthalmitis after cataract surgery. The efficacy of the combination of vancomycin and gentamycin has been reported to cov-

er almost all of causative strains of postoperative endophthalmitis (31). We observed that all of gram-positive microorganisms were sensitive to vancomycin. Although the causative agent (*Staphylococcus epidermidis*) was sensitive to both preoperative and intraoperative antibiotics they didn't prevent the development of endophthalmitis in this study. In addition, we do not know the exact value of topically applied ofloxacin (0.3%) for prophylaxis of postoperative endophthalmitis. Montan et al reported that intracameral cefuroxime 1 mg, which was safe and sufficient to achieve high antibiotic concentrations in the immediate postoperative period was of prophylactic value for postoperative endophthalmitis (32, 33). These findings suggested to us to consider the cost and the ecological effect of intravitreal vancomycin and 4-week ofloxacin (0.3%) therapy for future studies. We found that eyes with posterior capsular rupture had higher contamination rates than those eyes without posterior capsular rupture. Likewise, the type of microorganism was similar between aqueous samples and conjunctival smear in eyes with capsular rupture, comprising coagulase-negative staphylococcus in 12 out of 16 eyes (75%) with posterior capsular rupture in group 1. The eyes with postoperative endophthalmitis had also been complicated by posterior capsular rupture during the operation. Since eyes with posterior capsular rupture during the surgery had longer operation time and a

higher contamination rate, it seems reasonable to assume that increase in operation time would lead to the lessening of the preventive effect of intraocular antibiotics on colonization, and that several instrumental entries in this complicated eye would lead to more bacterial loading. It was reported that posterior capsular rupture compromises the ability of the eye to clear bacteria (34).

In conclusion, this study suggests that intraoperative antibiotic irrigation may decrease the rate of aqueous humor contamination in phacoemulsification surgery. Intraoperative posterior capsular rupture increased the risk of aqueous humor contamination. Considering the incidence of lower postoperative endophthalmitis with variable results, further studies are needed to determine whether there is a causal relationship between aqueous humor contamination and endophthalmitis in eyes with posterior capsular rupture.

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