Lack of Effect of Prophylactic Gentamicin Treatment on Intraocular and Extraocular Fluid Cultures After Pars Plana Vitrectomy

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■ BACKGROUND AND OBJECTIVE: To analyze the effect of preoperative prophylactic 0.3% gentamicin sulfate eyedrops on intraocular and extraocular fluid cultures after pars plana vitrectomy.

■ PATIENTS AND METHODS: Forty consecutive patients undergoing pars plana vitrectomy were randomly assigned to receive either 0.3% gentamicin eyedrops or placebo preoperatively. Fluids from the vitreous cavity and from the conjunctival sac were collected for bacteriologic studies.

■ RESULTS: Positive cultures from extraocular fluids were obtained in 30.4% of the gentamicin group and 35.3% of the placebo group (P = .75). Furthermore, 1 (3%) of 40 cultures of intraocular fluid and 13 (33%) of 40 cultures of extraocular fluid were positive. Culture growth positivity was not influenced by the patients' age, by diabetes, or by the duration of the operation.

■ CONCLUSIONS: Prophylactic gentamicin treatment by the method applied in this study is not effective on reducing growth positivity. Contaminated extraocular fluid may play an important role in the pathogenesis of bacterial endophthalmitis following pars plana vitrectomy.


INTRODUCTION

Postoperative bacterial endophthalmitis is a severe complication of intraocular surgery. Its incidence following pars plana vitrectomy is reported to be between 0.051% and 0.15%.1-4 The pathogenesis of postoperative bacterial endophthalmitis is not fully understood. Sherwood et al.5 found that in 90% of patients undergoing extracapsular cataract extraction, the extraocular fluid from the conjunctival sac was contaminated; as this fluid penetrated the eye during the operation, it led to contamination of the intraocular fluid in 29% of the cases. Pars plana vitrectomy is usually a longer operation than cataract extraction. This may increase the chances of extraocular fluid contamination during the operation. Cohen et al.6 reported that in 6% of 33 consecutive patients undergoing pars plana vitrectomy, bacterial cultures of vitreous aspirates were positive. In that study, however, extraocular fluid cultures were not performed.

Because routine perioperative antibiotic prophylaxis is intended to reduce microbial contamination during surgery7,8 the present prospective double-blind randomized study was designed to analyze the effect of preoperative gentamicin eyedrops on intraocular and
extraocular fluid contamination during pars plana vitrectomy.

PATIENTS AND METHODS

Forty consecutive patients (26 males and 14 females) undergoing pars plana vitrectomy in our department participated in this study. Ages ranged between 17 and 87 years (mean 60.5 years). Patients were excluded if they had evidence of local or systemic infection, recent penetrating ocular injury, or recent antibiotic or steroid treatment.

Patients were randomly assigned to receive either 0.3% gentamicin sulfate in povidone hydroxyethylcellulose eyedrops (gentamicin group) or povidone hydroxyethylcellulose eyedrops alone (placebo group), in identical bottles. Four eyedrops were applied preoperatively at 120, 60, 30, and 5 minutes each before the patient was transferred to the operating room.

All patients were fully informed and gave a written consent before being entered into the study, which met with local hospital ethics committee approval. Gentamicin was chosen for this study because it is still widely used for prophylaxis, and has been proven superior to many other drugs. A more potent antibiotic drug (e.g., fluoroquinolone) was not chosen because we believe that expensive first-line drugs should be reserved for treatment of severe ocular infections, and not for prophylaxis.

The operations were performed in the same room by two of us (YAG or BM). The patients' eyelids and the surrounding skin were scrubbed with 10% povidone-iodine for 3 minutes. No povidone-iodine was placed in the conjunctival sac. The skin was then dried with a sterile gauze. A plastic bag with an adhesive band was attached to the skin below the outer canthus for collection of extracellular fluid. The eyelids were then opened, and a plastic adhesive drape was applied over the eye and the inner wall of the collecting bag. The drape was incised over the globe, and an eyelid speculum was introduced with special care to tuck the edges of the drape around the lid margins.

A standard three-port pars plana vitrectomy was performed in each case. At the end of the operation, 2 ml of fluid was removed from the midvitreous cavity using a 20-gauge cannula. The aspirated fluid was immediately injected into two commercially available blood culture bottles (1 ml into each bottle) for testing for aerobic and anaerobic organisms, respectively. At the end of the operation, 10 ml of extracellular fluid was aspirated from the collecting bag and was immediately injected into two additional blood culture bottles (5 ml into each bottle) for aerobic and anaerobic testing. On completion of the fluid collection, the bottles were immediately transferred to our microbiology laboratory.

The use of commercially available blood culture bottles has been proven to be an efficient culture method for infectious endophthalmitis. BacTAlert culture bottles for aerobic and anaerobic bacterial growth (Organon Teknika Corp., Durham, NC) were used in this study. The bottles were incubated under constant agitation for 6 days at 37°C in a microbial detecting system (Organon Teknika Corp.). During this time the bottles were screened colorimetrically for bacterial growth every 10 minutes. If bacterial growth was colorimetrically detected, a sample from the bottle's liquid medium was stained with Gram and Giemsa. The culture medium from the bottle was then plated, according to the staining results, on standard culture media for final bacterial identification.

Statistical analysis was performed using the SPSS-PC program (SPSS Inc., Chicago, IL). We used the Student's t test, the Pearson test, or logistic regression analysis to examine statistically significant associations.

RESULTS

The indications for vitrectomy were complications of proliferative diabetic retinopathy in 17 patients, proliferative vitreoretinopathy in 14, macular hole in 4, vitreous hemorrhage complicating branch vein occlusion in 2, macular pucker in 1, removal of dislocated lens from the vitreous in 1, and asteroid hyalosis in 1. The operations lasted between 0.7 and 3.5 hours (average duration 1.89 [SD 0.74] minutes).

Patient data and results are summarized in the table. There were 23 patients in the gentamicin group and 17 patients in the placebo group. These groups were similar in mean age, prevalence of diabetes, and mean duration of the operation. Prophylactic treatment with gentamicin eyedrops had no effect on culture growth positivity from intraocular and extraocular fluids. Seven (30.4%) of 23 cultures of extraocular fluids were positive in the gentamicin group, compared with 6 (35.3%) of 17 cultures of extraocular fluids in the placebo group (P = .75). Only 1 patient had a positive culture from the eye fluid. This was a diabetic patient who received prophylactic gentamicin.
treatment and did not have postoperative bacterial endophthalmitis.

Analyzing the patients as one group, 1 (3%) of 40 intraocular fluid cultures was positive (*Staphylococcus* coagulase negative), and 13 (33%) of 40 extraocular fluid cultures were positive. One extraocular fluid culture grew *Citrobacter* and the other 12 cultures grew *Staphylococcus* coagulase negative (with 1 of these cultures growing a mixture containing *Escherichia coli* as well). No bacteria were recovered from any of the anaerobic blood cultures bottles.

Logistic regression analysis revealed no effect of age, presence of diabetes, or duration of the operation on the culture growth positivity of extraocular fluids.

**DISCUSSION**

Although the preponderance of evidence shows that perioperative prophylactic antibiotic treatment may reduce the incidence of postoperative bacterial endophthalmitis, the timing and the optimal route of administration are not well established. As no study in the ophthalmic literature has satisfactorily been designed or executed to convincingly address these issues, we have to rely on the principles learned from the study of wound infections in general surgical procedures. Because it is not possible to sterilize the conjunctival sac, preoperative topical antibiotic prophylaxis is intended to significantly reduce the number of the bacteria there. Long preoperative treatment (e.g., eyedrops applied for 3 days preoperatively) carries the advantage of exposing the conjunctival bacterial flora to bactericidal concentrations of antibiotics for a long period in order to exert a maximal effect. This treatment, however, contradicts the principles of prophylaxis, as applied from general surgery, because it increases the likelihood of promoting antibiotic resistance and superinfections. Short prophylactic treatment commencing 2 hours preoperatively, as applied in our study, carries the risk of insufficient time exposure of the conjunctival bacterial flora to the antibiotic drug. However, this timing of prophylaxis is in accordance with the general principles of prophylaxis, and it is also supported by a large study of general surgery patients that found that the optimal timing for prophylactic antibiotic administration is 2 hours before the operation.

Furthermore, bacterial time-kill studies have shown that aminoglycosides that act by interfering with protein synthesis (such as gentamicin, which was chosen in our study) produce a far more rapid bactericidal effect than antibiotics that interfere with cell wall synthesis, and are therefore more suitable for short preoperative prophylactic treatment.

Based on the above-mentioned data, gentamicin eyedrops (or placebo) were applied in our study beginning 2 hours preoperatively. This treatment had no effect on the contamination of intraocular and extraocular fluids (see the table). The percentage of contaminated extraocular fluids was 30.4% in the gentamicin group, compared with 35.3% in the placebo group. In the case of intraocular fluids, 1 of 40 cultures (a case that belonged to the gentamicin group) was positive for bacterial growth. Thus, short preoperative topical gentamicin treatment cannot prevent bacterial contamination during surgery. This conclusion is supported by another double-blind randomized study that found preoperative prophylactic topical norfloxacin treatment to have no effect on bacterial contamination of anterior chamber aspirates following cataract surgery. In that study, however, extraocular fluids were not analyzed.

Our study confirms that intraocular bacterial contamination is less common during pars plana vitrectomy than during extracapsular cataract extraction. Only 3% of intraocular fluid samples were found to be contaminated, compared with 6% reported by Cohen et al. This percentage is much lower than that obtained from anterior chamber aspira-
rates in extracapsular cataract operations, which have been reported to be as high as 24% to 43%.\textsuperscript{5,16,17}

In the present study, 33% of the fluid samples that originated from the conjunctival sac were contaminated. This percentage of contamination is lower than the 90% described by Sherwood et al.\textsuperscript{5} during cataract surgery, although different culture techniques were used. Both results show that one of the main sources of intraocular bacterial contamination originates from contaminated extracocular fluids. Using fluorescein dye, Sherwood et al.\textsuperscript{5} demonstrated persistent penetration of extracocular fluids into the anterior chamber during extracapsular lens extraction. It is logical to assume that because of the small sclerotomies and the positive intraocular pressure throughout the operation, smaller amounts of extracocular fluid can penetrate the eye during pars plana vitrectomy. This may explain the higher ratio of intraocular to extracocular fluid contamination (1:3) in extracapsular cataract extraction (Sherwood et al.'s study) compared with a rate of 1:10 in pars plana vitrectomy (our study), and may provide a possible explanation for the lower incidence of postoperative bacterial endophthalmitis after pars plana vitrectomy compared with cataract surgery.

Logistic regression analysis showed that extracocular fluid contamination was not influenced by the duration of the operation, nor by the patients' age and the presence of diabetes. Contaminating bacteria have been claimed to originate from various sources. It seems, however, that the main sources of contamination are the patients' surface tissues\textsuperscript{18} as well as airborne contamination originating from various sources, including the surgeon and the operating room personnel.\textsuperscript{19,20} Low concentrations of antibiotics in the irrigating solutions (gentamicin 8 \( \mu \)g/ml with or without 20 \( \mu \)g/ml of vancomycin) are intended to prevent intraoperative intraocular contamination (regardless of its source) without causing intraocular antibiotic toxicity. This relatively new prophylactic treatment is controversial; despite the fact that early reports demonstrated the efficiency of such treatment,\textsuperscript{21-23} a later report failed to confirm it.\textsuperscript{24}

Routine perioperative prophylaxis is intended to reduce the risk of bacterial contamination during the operation. In the present study, preoperative prophylactic 0.3% gentamicin sulfate eyedrops failed to prevent intraocular and extraocular fluid contamination during pars plana vitrectomy. Further studies are required to analyze the efficiency of other known routes, different timing, and other types of antibiotics for prophylaxis.

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