Intracameral Antibiotics and Cataract Surgery: Endophthalmitis Rates, Costs, and Stewardship

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Acute-onset postoperative endophthalmitis is a rare but vision-threatening complication of cataract surgery. The incidence rate varies substantially in the literature but is generally reported in the range of 0.03% to 0.2%. In the current issue of *Ophthalmology*, Creuzot-Garcher et al report a retrospective series of 6,371,242 phacoemulsification surgeries in which the rate of endophthalmitis declined from 0.145% to 0.053% over a 10-year period (see page XXX). During this timeframe, the use of intracameral antibiotics increased from 0.60% to 80.03%, and the investigators concluded that the intracameral antibiotics were responsible for these outcomes.2

These results are intriguing and illustrate the power of “Big Data” medical record analyses. However, as the authors acknowledge, all “Big Data” studies are limited by their retrospective nature and potential inaccuracies in diagnosis and procedure coding.3 Other recent series also have reported significant associations between intracameral antibiotics and lower rates of endophthalmitis.4-6 However, many of these studies were flawed by comparing rates in patients undergoing operations during an earlier timeframe (not receiving intracameral antibiotics) with those of different patients undergoing operations during a later timeframe (receiving intracameral antibiotics). Many other factors could explain the decreased rates of endophthalmitis over time, including improvements in equipment, surgical techniques, topical antibiotics, and unknown factors.7 In addition, not all such series reported benefits associated with intracameral antibiotics. For example, a prospective comparative interventional cohort study compared patients undergoing operation during an earlier timeframe (without intracameral antibiotics) with patients undergoing operation during a subsequent timeframe (with intracameral antibiotics) and reported no significant differences.8

The highest-quality evidence comes from randomized clinical trials (RCTs) rather than observational studies. The only RCT specifically designed to answer this question was conducted by the European Society of Cataract and Refractive Surgeons (ESCRS), which randomized patients into 4 treatment arms and reported an approximately 5-fold reduction in endophthalmitis rates associated with intracameral cefuroxime.9 However, the endophthalmitis rates among patients in the 2 arms not treated with intracameral cefuroxime were relatively high (0.18% and 0.23%), which may have exaggerated the apparent benefits of antibiotics. Other series from similar timeframes have reported low rates of endophthalmitis without the use of intracameral antibiotics. For example, Lalitha et al10 reported an endophthalmitis rate of 0.05% in a retrospective series including 22,294 phacoemulsifications and 9,503 extracapsular extractions. Likewise, Moshirfar et al11 reported a rate of 0.07% in a retrospective study of 20,013 phacoemulsifications.

There are other concerns about the ESCRs study, including the use of multiple different surgical techniques12 and the use of topical levofloxacin, rather than fourth-generation fluoroquinolones.7

Povidone-iodine antisepsis is the only technique to reach category II evidence in reducing endophthalmitis rates.13 In contrast, intracameral antibiotics are unproven and associated with increased costs, as well as risks of overdoses, contaminants, and increased bacterial resistance.14 Overdoses of intracameral cefuroxime are associated with macular edema, retinal vascular leakage, and uveitis,15 as well as endothelial toxicity and toxic anterior segment syndrome.16 In one report, 7 consecutive patients developed endophthalmitis caused by *Fusarium* species after the use of intracameral cefuroxime.17 Intracameral vancomycin is associated with postoperative hemorrhagic occlusive retinal vasculitis and severe visual loss.18 Some of these risks may be ameliorated with the use of a prepackaged cefuroxime indicated for intracameral use (Aprokam, Thea Pharmaceuticals, Clermont-Ferrand, France), but this agent is not available in the United States, and its adoption is variable even in nations where it is approved.19

Additional insights may be obtained by considering the number needed to treat, defined as the average number of patients who must be exposed to an intervention to prevent 1 unfavorable outcome.20 As an example, Lalitha et al20 and Moshirfar et al11 reported rates of approximately 0.06% without intracameral antibiotics. By assuming that the 3-fold reduction in endophthalmitis rates reported by Creuzot-Garcher et al2 is “true,” this implies that if these centers
started using intracameral antibiotics, the endophthalmitis rate could be reduced from approximately 6/10000 to 2/10000. Therefore, it would be necessary to treat approximately 2500 patients with antibiotics to prevent 1 additional case of endophthalmitis. If the antibiotics cost $100, these extra 2500 doses would cost a quarter of a million dollars, in addition to the risks of the antibiotics themselves.

It is estimated that more than 50% of antibiotic use is unnecessary or inappropriate, and antibiotic stewardship programs aim to improve these practices. In 1995, the Centers for Disease Control guidelines discouraged the routine use of vancomycin in surgical prophylaxis. In addition, drug resistance is an important clinical challenge, illustrated by the increasing resistance of coagulase-negative *Staphylococcus* to fluoroquinolones and cephalosporins. Widespread use of intracameral antibiotics for cataract surgery is contrary to the basic thesis of antibiotic stewardship.

The role of intracameral antibiotics remains controversial in the United States and in many other nations. The only published RCT (by the ESCRS) is limited by the relatively high rates of endophthalmitis in eyes not randomized to receive intracameral cefuroxime, as well as flaws in the study design. Many observational series, including the study by Creuzot-Garcher et al., are limited by their retrospective and nonrandomized study designs. The use of intracameral antibiotics should not be considered “standard of care” in the United States, and the value of this strategy remains uncertain on the basis of currently available data.

References

Supported in part from the National Institutes of Health Center Core Grant P30EY014801 (Bethesda, MD), Research to Prevent Blindness Unrestricted Grant (New York, NY), and the Department of Defense grant no. W81XWH-09-1-0675 (Washington, DC).

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