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Is It Time to Abandon Subconjunctival Antibiotics at the Time of Pars Plana Vitrectomy?

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The use of subconjunctival antibiotics has been a routine part of endophthalmitis prophylaxis at the end of ophthalmic procedures for decades.^{1–4} Subconjunctival antibiotics are used to provide an additional drug reservoir for extended duration during the postoperative period and enhance microbial eradication.⁵ Dating back fifty years, case series reported very low rates of endophthalmitis following cataract surgery using subconjunctival antibiotics, and yet its use more recently has greatly fallen. In a 2014 the American Society of Cataract and Refractive Surgery (ASCRS) members survey, only 8% reported use of prophylactic subconjunctival antibiotics during cataract surgery in part due to increased use of prophylactic intracameral and topical antibiotics.⁶ Most cataract surgeons have abandoned this practice partly because of a switch to intracameral and topical antibiotics. The switch to intracameral antibiotic prophylaxis is not without controversy. While there is some evidence of efficacy, the complications (Hemorrhagic occlusive retinal vasculitis and antibiotic mixing errors among other complications) might outweigh the benefits. In view of the apparent lack of efficacy, the potential for complications and the need for stewardship of antibiotic use the use of subconjunctival antibiotics for endophthalmitis prophylaxis during intravitreal injections is abandoned and is not necessary during vitrectomy.

When pars plana vitrectomy (PPV) surgery began in the 1970's, the use of subconjunctival antibiotics was routinely performed and was thought to be the standard of care for all intraocular surgeries. In the current issue of *RETINA*, Weiss et al report a retrospective case series of 18,886 PPV patients in which the rate of post-operative endophthalmitis was not statistically different between those treated with subconjunctival antibiotics (0.078%) and those with none (0.10%).⁷ This was not a randomized prospective multicenter clinical trial but these data suggest that the use of subconjunctival antibiotics needs to be reconsidered. Antibiotics like other medications have risks, benefits, and costs.^{8,9} Given need to balance these issues, it is important that we examine more closely our current antibiotic practices.

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Though rare, the outcomes of postoperative endophthalmitis can be devastating. Various antimicrobial agents have been employed to theoretically reduce endophthalmitis rates. Prophylactic antibiotics may play a role in the success of this endeavor, but these agents are used in many ways that are not evidence based. Antisepsis with povidone-iodine is the only practice with category II evidence in reducing the rates of postoperative endophthalmitis.¹⁰ In an open-label nonrandomized parallel trial by Speaker et al, the incidence of culture-positive endophthalmitis after intraocular surgery during 11-month study period were lower from the operating rooms where topical 5% povidone-iodine was used (2 of 3489 or 0.06%) compared to the rates from operating rooms where silver protein solution was used (11 of 4594 or 0.24%).¹¹

Endophthalmitis after pars plana vitrectomy (PPV) is rare but may be associated with poor visual outcomes. In a review by Dave et al, the incidence rates of endophthalmitis after 20-G PPV were found to be 0.02% to 0.15%.¹² In 2 different case series (Ho et al, 1984 and Cohen et al, 1995), the endophthalmitis incidence rates after 20-gauge vitrectomy were reported as 0.14% (4/2,800) and 0.07% (9/12,216) respectively.^{13, 14} Cohen et al (larger of the two case series) reported that 14/18 of the endophthalmitis cases occurred despite prophylactic subconjunctival antibiotics.¹⁴

Case series of 23- and 25-gauge vitrectomies were associated with slightly higher endophthalmitis rates in earlier reports.^{15, 16} In other series, the rates of endophthalmitis after transconjunctival small gauge vitrectomy (23G-, 25G-, and 27G-) were reported to be between 0.03% to 1.55%.^{12, 17} A Microsurgical Safety Task Force investigated the risk factors for postoperative infection and proposed guidelines that might reduce the rates of endophthalmitis post PPV.¹⁸ Regarding prophylaxis practices, the Task Force emphasized the use of preoperative iodine as a measure proven to decrease endophthalmitis rates after cataract surgery. Regarding subconjunctival antibiotics, they stated that “it was reasonable either to use or to forgo perioperative antibiotic injections” due to lack of higher levels of evidence.^{18, 19} A subsequent meta-analysis as well as follow-up studies reported that the endophthalmitis rates among 20- and 25-gauge PPV were not statistically different.^{20, 21} The changes in these rates were largely attributed to changes in surgical techniques aligned with the recommendations from the Task Force.

In scleral buckling procedures, the use of perioperative subconjunctival antibiotics has been examined. One series of 2972 cases reported a statistically significant reduction in infection or extrusion when the buckle itself was soaked in antibiotics during surgery.²² However, a more recent 11-year analysis of 1127 cases demonstrated that soaking the buckle in gentamycin and irrigating the scleral surface intraoperatively had no effect on the rates of infection or extrusion.²³

In addition to its use in prophylaxis, subconjunctival antibiotics have been traditionally employed in the treatment of infectious endophthalmitis. In a retrospective cohort study by Iyer et al, subconjunctival antibiotic injection was reported to be not associated with treatment benefit in patients with acute postoperative endophthalmitis presenting with vision of hand motions or better.²⁴ In another retrospective, nonrandomized consecutive series of 54 patients with clinically diagnosed bacterial endophthalmitis confirmed with positive

cultures, the authors reported no statistically significant differences in final visual acuity and reinjection rates among two study groups (subconjunctival antibiotics used [group ABX; n = 21] or not used [group noABX; n = 33]) during management.⁵ These studies indicate that subconjunctival antibiotics may not be necessary to treat infectious endophthalmitis managed with standard tap and injection or vitrectomy techniques.

As with any procedures, the injection of subconjunctival antibiotics is not without risks. Reports of anaphylaxis and globe penetration highlight the potential complications.^{25, 26} Subconjunctival injection of cefazolin (50mg) lead to anaphylaxis in a 70-year-old female who needed to be intubated and eventually recovered with intensive care.²⁵ A case of corneal opacification immediately after subconjunctival injection of soframycin antibiotic was reported at the end of bilateral goniotomy procedure performed for buphthalmos.²⁶

No single antibiotic is effective for coverage of all microbes isolated from eyes with endophthalmitis.^{27, 28} Since gram-positive organisms are the most common isolates in postoperative endophthalmitis, vancomycin would be a logical choice for prophylaxis. However, the Centers for Disease Control and Prevention (CDC) warns that vancomycin should not be used as a prophylactic antibiotic.²⁹ In the series by Weiss et al, intraoperative subconjunctival antibiotics (vancomycin 50mg/ml or cefazolin 330mg/ml) were utilized in the management of cases undergoing PPV.⁷ Based on these CDC guidelines, using vancomycin prophylaxis is strongly discouraged. The CDC estimates that one-half of the time, antibiotics are misused or used when not needed.³⁰ The onus is on the physician to ensure that antimicrobials are used appropriately and judiciously in order to reduce the emergence of antimicrobial resistance. Antibiotic stewardship programs mandated by Centers for Medicare and Medicaid Services and the new medication management standards (MM.09.01.01) are increasingly important in today's regulatory environment.⁹

The costs to patients and the health care system are high. Apart from the possible emergence of resistance, use of subconjunctival antibiotics on a scale necessary for the increasing number of vitrectomies in the US exerts a huge cost burden on the medical system as a whole. Subconjunctival antibiotics may be associated with additional patient discomfort and increased cost of treatment.⁵

As stated by Weiss et al, routine perioperative subconjunctival antibiotics may not reduce the rate of endophthalmitis.⁷ This conclusion will be confirmed by ongoing clinical experience in view of the large number of PPV procedure performed worldwide. In our opinion, this is time to abandon subconjunctival antibiotics after PPV.

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Summary Statement

Prophylactic subconjunctival antibiotics at the end of ophthalmic procedures has been a traditional standard of care. In view of risks and costs with questionable benefit, subconjunctival antibiotics may be eliminated as part of pars plana vitrectomy procedures.