ENDOPHTHALMITIS AFTER TRANSCONJUNCTIVAL PARS PLANA VITRECTOMY

A 6-year Experience Without Prophylactic Intraoperative Subconjunctival Antibiotics

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Purpose: This study aimed to investigate the incidence and risk factors of endophthalmitis after transconjunctival pars plana vitrectomy (PPV) without intraoperative subconjunctival antibiotics.

Design: Retrospective, consecutive case series at a single institution.

Methods: Consecutive cases of transconjunctival 25-gauge PPV without intraoperative subconjunctival antibiotics performed by three retina surgeons at a single surgical site at the Dean McGee Eye Institute from 2012 to 2018 were reviewed.

Results: Of 4,263 cases of PPV without intraoperative subconjunctival antibiotics, five cases (0.117%, 5/4,263) of post-PPV endophthalmitis were identified. Of these five cases, four cases (80%, 4/5) received combined cataract extraction or secondary intraocular lens implantation at the time of PPV. The incidence of endophthalmitis in isolated PPV was 0.027% (1/3,606 cases), whereas the incidence in combined PPV with anterior segment procedures was 0.608% (4/657 cases). Risk factors for endophthalmitis included diabetes mellitus, which was present in 80% of patients with endophthalmitis (4/5 cases). Causative organisms were identified in four of the five cases (80%), including *Staphylococcus epidermidis* (N = 3) and *Propionibacterium acnes* (N = 1).

Conclusion: Performing transconjunctival PPV alone with standard preparation using povidone-iodine and postoperative topical antibiotics for 1 week without intraoperative subconjunctival antibiotics did not lead to an increase in incidence of postoperative endophthalmitis (1 per 3,606 cases).

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Postoperative endophthalmitis after ocular surgery is relatively rare; reportedly, 0.4 to 1.3 per 1,000 cases (0.04%–0.133%) after cataract extraction (CE) and 0.1 to 1.4 per 1,000 cases (0.018%–0.14%) after pars plana vitrectomy (PPV).^{1–10} However, it is one of the most serious complications after ocular surgery. Therefore, preventing postoperative endophthalmitis is important to every ophthalmic surgeon. Among various approaches to prevent postoperative endophthalmitis, intraoperative prophylactic subconjunctival antibiotics have been traditionally used to prevent endophthalmitis at the end of ocular surgery, although evidence supporting this practice is weak. Over the past decade, most cataract surgeons switched from subconjunctival antibiotics to topical antibiotics or intracameral antibiotics, but the use of subconjunctival prophylactic antibiotics during PPV has remained a standard procedure for many retina surgeons due to the lack of definitive guidelines.^{11–13}

To date, there have been limited studies evaluating the rate of post-PPV endophthalmitis with or without subconjunctival antibiotics. Weiss et al recently reported that the rate of postoperative endophthalmitis was not statistically different between those treated with subconjunctival antibiotics (0.78/1,000 cases; 0.078%) and those without subconjunctival antibiotic treatment (1/1,000 cases; 0.10%). The authors suggested that it is time to reconsider routine prophylactic antibiotics practices during the PPV.⁷ Because of the rare incidence of post-PPV endophthalmitis, controlled studies of prophylactic antibiotics are challenging to perform and would require very large numbers to obtain statistical significance. For instance, a cohort of nearly 180,000 is needed to detect the difference between the two groups with incidence of 0.1% and 0.05%, respectively, with 80% power and a 0.05 significance level.

Since 2012, our institution as a tertiary medical center has gradually adopted the approach of no intraoperative antibiotics prophylaxis during PPV because of lack of scientific evidence, patient discomfort, and cost-effectiveness. The institutional surgical center closely monitors the occurrence of post-PPV endophthalmitis. The purpose of this study was to report the incidence and risk factors of endophthalmitis after transconjunctival PPV without intraoperative subconjunctival antibiotics.

METHODS

This is a retrospective consecutive case series of transconjunctival 25-gauge (G) PPV without intraoperative subconjunctival antibiotics conducted from July 1, 2012, to December 31, 2018, at the Dean McGee Eye Institute (DMEI). This study adhered to the tenets of the Declaration of Helsinki. Approval was obtained from the Institutional Review Board of the University of Oklahoma Health Sciences Center before conducting the study. All cases were performed at the McGee Eye Surgery Center (MESC), an ambulatory surgical center, and were performed by one of three vitreoretinal surgeons at the DMEI.

Inclusion criteria were primary PPV, cases of PPV combined with scleral buckle procedure, and cases of PPV performed in combination with CE, intraocular lens removal, and/or intraocular lens replacement without prophylactic intraoperative subconjunctival antibiotics administration. Pars plana vitrectomy included pars plana lensenctomy requiring removal of either retained lens materials after cataract surgery or dislocated crystalline lens by either a 25 G vitrectomy cutter or by using a fragmatome by extending the same 25 G sclerotomy wound. Exclusion criteria included preexisting endophthalmitis or penetrating trauma.

As a routine preoperative eye preparation, the periorbital skin and lashes of all eyes were scrubbed in a progressively outward circular motion using sterile gloves and sterile gauze pads soaked in 10% povidoneiodine, in addition to a conjunctival irrigation using 5% povidone-iodine before the operating sterile field was prepared. Patients were draped, and the lashes were everted and covered to prevent contamination of the operative field. No talking policies were applied. During the operation, standard surgical instrumentation, including disposable sterile vitrectomy probe sets and autoclaved surgical instruments, was used. No antibiotic was added to the infusion fluid. All sclerotomy sites from 25 G PPV were evaluated for leakage after cannula removal at the completion of each case. Scleral wound was closed using either 7-0 or 8-0 Vicryl sutures at the discretion of the operating surgeon if leakage was noted. Neither subconjunctival antibiotics nor steroids were given at the end of the operation. All patients received topical antibiotic and/or steroid drops or ointment before patching at the conclusion of the case. All patients routinely received postoperative topical ofloxacin ophthalmic solution 0.3% four times a day for 1 week and prednisolone acetate 1% four times a day for 1 week, followed by a taper for 2 to 3 weeks. For the combined anterior segment surgery, corneal wounds were sutured with either 8-0 Vicryl or 10-0 nylon sutures in all cases. No wound leak was confirmed before proceeding and at the end of PPV.

Cases of postoperative endophthalmitis were diagnosed within 4 weeks of surgery by clinical findings, including decreased vision, pain, fibrin and/or hypopyon, and vitritis, and defined as those who received vitreous tap with intraocular injection of antibiotics, regardless of microbiological evidence. Statistical analysis was performed using SAS 9.4. *P* values of less than 0.05 were considered statistically significant. For all rates, 95% Bernoulli confidence intervals (CIs) were calculated.

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RESULTS

Over the 6-year study period, 4,263 consecutive 25 G PPVs without prophylactic intraoperative subconjunctival antibiotics administration were performed. The mean age of individuals included in the study was 58.1 years (SD 16.9). Of these patients, 2,428 were men and 1,835 were women. Indications for PPV were retinal detachment (1,760 eyes, 41.3%); macular surgery, including epiretinal membrane and macular hole (1,351 eyes, 31.7%); diabetic eye disease, including vitreous hemorrhage, tractional retinal detachment, or both (967 eyes, 22.7%); retained lens (54 eyes, 1.3%); and silicone oil removal (131 eyes, 3.1%). The retained lens including retained lens materials after cataract surgery or dislocated crystalline lens was removed by either a 25 G vitrectomy cutter or by using a fragmatome by extending the same 25 G sclerotomy wound. Of the 4,263 cases, 657 had combined anterior segment procedures. These combined procedures included CE (492/657 eyes) and intraocular lens placement, with or without lens removal (165/657 eyes) (Table 1).

Five cases of postoperative endophthalmitis were identified from 4.263 PPV cases without prophylactic intraoperative subconjunctival antibiotics (5/4,263 eyes, 1.17 per 1,000 cases; 0.117%) (Table 2). The average number of days until onset of symptoms from postoperative endophthalmitis was 3.8 (range of 3-6 days after PPV). The visual acuity for each patient when endophthalmitis presented varied from bare light perception to 20/100 was as follows: 2 patients had (B) LP, two patients had HM, and one patient had visual acuity 20/100. All five patients received immediate vitreous tap with intraocular injection of antibiotics: vancomycin (1 mg/0.1 mL) and ceftazidime (2.25 mg/0.1 mL). Two patients underwent repeat PPV for endophthalmitis (cases 4 and 5) (Table 2). Causative organisms, which included Staphylococcus epidermidis (N = 3) and Propionibacterium acnes (N= 1), were identified in four of the five (80%) cases. Indications for PPV in patients that developed endophthalmitis included diabetic retinopathy (60%, 3/5), dislocated crystalline lens (20%, 1/5), and epiretinal membrane (20%, 1/5). At the conclusion of management of postoperative endophthalmitis, final visual acuity for each patient ranged from no light perception to 20/30. Final visual acuity of two of the five endophthalmitis eves was better than 20/40 (40%) (Table 2).

Notably, of the five cases of endophthalmitis, four had combined anterior procedures, including CE (3/4 eyes) and lens placement (1/4 eyes). The incidence of post-PPV endophthalmitis in cases without prophylactic subconjunctival antibiotics after isolated PPV or com-

bined scleral buckle procedure alone was 0.27/1,000 cases; 0.027% (1/3,606 cases; 95% CI, 0%–0.082%). The incidence of post-PPV endophthalmitis in cases combined with anterior segment procedure was 6/1,000 cases; 0.608% (4/657 cases; 95% CI, 0.014%–1.204%).

A combined anterior segment procedure was performed by anterior segment surgeons at the DMEI. At the conclusion of the anterior segment procedure, all corneal wounds were sutured. No prophylactic intraoperative antibiotics were given to these patients. Of the five cases of post-PPV endophthalmitis, four had underlying diabetes (4/5, 80%). Three of four patients with diabetes had underlying proliferative diabetic retinopathy, and two of four patients with diabetes had poorly controlled diabetes with hemoglobin A1c (HbA1c) more than 9% (Table 2).

From the transitional period at our institution, 814 cases that received prophylactic subconjunctival antibiotics were identified. Of 814 cases with prophylactic subconjunctival antibiotics, 668 cases underwent isolated PPV and 146 cases underwent PPV combined with anterior segment procedures. One case of postoperative endophthalmitis of the 814 cases was identified in this subgroup. Interestingly, the endophthalmitis case after PPV with prophylactic subconjunctival antibiotics was a case performed with a combined anterior segment procedure. We did not compare the incidence of endophthalmitis between the two groups due to the imbalance between cases receiving or not receiving prophylactic subconjunctival antibiotics (N = 4,263 and 814, respectively).

DISCUSSION

Intraoperative prophylactic subconjunctival antibiotics have been traditionally used to prevent post-PPV endophthalmitis, without any definitive evidence. The use of subconjunctival prophylactic antibiotics has remained a standard procedure for many retina surgeons due to the lack of definitive guidelines. The Microsurgical Safety Task Force was convened to evaluate the evidence and to address guidelines to minimize the rates of endophthalmitis by the panels from the multicenter vitreoretinal surgical experts, when transconjunctival small-gauge vitrectomy was introduced.^{12,13} It emphasized the use of preoperative povidone-iodine; however, the guidelines for usage of prophylactic subconjunctival antibiotics were inconclusive, stating that, "although all members of the task force use subconjunctival antibiotics at the conclusion of surgery, there was broad agreement that it is reasonable if a surgeon chooses not to use them because there is no scientific evidence."12,13 It has been challenging

Demographics			
Mean age Gender	58.1 ± 16.9 years 2,428 male; 1,835 female		
Clinical features	No. of cases (%)		
No. of cases (25 G PPV) without subconjunctival abx Isolated PPV ± scleral buckle Combined anterior segment procedure CE and IOL IOL ± removal of IOL or retained lens material Indication for PPV Diabetic eye disease Retinal detachment Macular surgery Silicone oil removal Retained lens Presence of diabetes	4,263 3,606 657 492 165 967 (22.7%) 1760 (41.3%) 1,351 (31.7%) 131 (3.1%) 54 (1.3%) 1 272 (29.8%)		
No. of cases	No. of endophthalmitis (incidence, Cl)		
Total PPV, $N = 4,263$ Isolated PPV, $N = 3,606$ Combined PPV and anterior segment procedures, $N = 657$	5 (0.117%; 95% Cl 0.015%–0.220%) 1 (0.027%; 95% Cl 0%–0.082%) 4 (0.608%; 95% Cl 0.014%–1.204%)		

Table 1.	Patient	Demographics	and	Clinical	Features
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abx, antibiotics; CE, cataract extraction; IOL, intraocualr lens.

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to perform controlled studies of prophylactic antibiotics because the incidence of acute infectious endophthalmitis after PPV is low.^{1–7}

During the initial period when the sutureless, transconjunctival, small-gauge PPV procedure was introduced, the incidence of post-PPV endophthalmitis after transconjunctival PPV was reportedly higher than that of 20 G PPV, reportedly 2.3 to 8.4 per 1,000 cases (0.23%–0.84%).^{3,4} Proposed explanations for the increased incidence included that nonsutured wounds may allow entry of extraocular fluids and organisms and that frequent hypotony observed after

Postoperative Endophthalmitis	Case 1	Case 2	Case 3	Case 4	Case 5
Preoperative and postoperative features					
Surgical procedure Surgical indication	PPV Diabetic TRD	PPV + CEIOL Diabetic VH	PPV + CEIOL ERM	PPV + CEIOL Diabetic VH	PPV + ACIOL Dislocated crystalline lens
VA before PPV Diabetes mellitus	20/800 Yes/PDR poorly controlled	20/40 Yes/PDR	20/50 Yes/No PDR poorly controlled	20/60 Yes/PDR	20/50 No
Postop hypotony Endophthalmitis	No	No	No	No	No
Duration until onset (days)	4	4	5	3	3
VA at time of endophthalmitis diagnosis	LP	20/100	BLP	HM	HM
Management of endophthalmitis Culture Final VA	Tap and inject S <i>. epidermidis</i> HM	Tap and inject <i>P. acn</i> es 20/30	Tap and inject <i>S. epidermidis</i> Prosthesis	Tap, inject, and PPV <i>No growth</i> LP	Tap, inject, and PPV <i>S. epidermidis</i> 20/40

Table 2. Clinical Characteristics of Endophthalmitis Cases

CEIOL, cataract extraction and intraocular lens insertion; ACIOL, anterior chamber intraocular lens; TRD, tractional retinal detachment; VH, vitreous hemorrhage; VA, visual acuity; ERM, epiretinal membrane; PDR, proliferative diabetic retinopathy; LP, light perception; BLP, bare light perception; HM, hand motion.

25 G PPV with reported incidence of 3.8% to 20% may serve as a conduit for infection.^{3,4} The reportedly increased incidence of post-PPV endophthalmitis after small-gauge PPV during the initial period may have been an additional concern to discontinue a common practice of using prophylactic antibiotics because sutureless transconjunctival small-gauge PPV has become a mainstream procedure over the past decade. However, with advancements in instrumentation and surgical technique as well as improved understanding of small-gauge vitrectomy wound construction, multiple reports support that the incidence of post-PPV endophthalmitis does not depend on the gauge used, ranging from 0.5 to 1.4 per 1,000 cases (0.054%-0.14%) in sutureless small-gauge PPV.¹³⁻¹⁶ In addition to proper wound construction, the use of antiseptics, such as povidone-iodine, is a perioperative preparation that is proven to reduce post-PPV endophthalmitis.^{12,13,17} Meanwhile, prophylactic subconjunctival antibiotics have remained a routine procedure for many retinal surgeons, without supporting scientific evidence.

In a large retrospective case series with 18,886 PPV cases, Weiss et al⁷ recently reported that the rate of postoperative endophthalmitis was not statistically different between those treated with subconjunctival antibiotics (0.7 per 1,000 cases [0.078%]; 11/14,068 cases) and those without subconjunctival antibiotic treatment (1.0 per 1.000 cases [0.10%]: 5/4.818 cases). Based on these findings, the authors suggested that the routine prophylactic injection of subconjunctival antibiotics may not reduce the postoperative endophthalmitis risk associated with transconjunctival PPV. To the best of our knowledge, Weiss's report is the first large-scale study that provided evidence that prophylactic subconjunctival antibiotics may not be necessary to prevent postoperative endophthalmitis after PPV. Although Weiss's report provides reasonable evidence for providers to reconsider routine prophylactic antibiotic practices, it was a retrospective study from a single institute. An examination of multicenter data would be necessary before one could consider abandoning prophylactic subconjunctival antibiotics during PPV. However, immediate data from randomized prospective multicenter clinical trials will not be available due to challenges associated with the low incidence of post-PPV endophthalmitis.

Since 2012, administration of subconjunctival antibiotics at the conclusion of PPV has been gradually discontinued at our institution because of lack of scientific evidence, patient discomfort, and costeffectiveness. Our results showed that the incidence of postoperative endophthalmitis after discontinuing prophylactic subconjunctival antibiotics (0.27 per 1,000 cases; 0.027%) remained low and was in fact lower than the known incidence in isolated transconjunctival PPV cases (0.5-1.4 per 1,000 cases; [0.054%-0.14%]).¹³⁻¹⁵ Our study cohort had relatively small-scale variations in surgeons performing the procedure because all procedures were performed by one of three experienced retina surgeons. Furthermore, endophthalmitis occurred in cases from each of the three surgeons, supporting that there was no surgeon bias. All cases received 25 G PPV at a single ambulatory surgical center with standardized preoperative preparation with 10% povidone-iodine and postoperative topical antibiotics and steroid usage with no subconjunctival steroid usage. Given the findings of this study, our cumulative clinical experience with transconjunctival PPV without the use of prophylactic antibiotics supports the recent findings by Weiss et al⁷ that prophylactic subconjunctival antibiotics may not be necessary to prevent postoperative endophthalmitis after transconjunctival PPV.

Further analyses of the five endophthalmitis cases demonstrated classic clinical characteristics of postoperative endophthalmitis, including infection with common organisms, such as *Staphylococcus epidermidis*, in three cases.¹⁸ Diabetes, which is a known risk factor for postoperative endophthalmitis, was also a significant risk factor in four of the five cases of postoperative endophthalmitis and poor control in two of the four diabetic patients.¹⁹ However, it was surprising to us that PPV combined with the anterior segment procedure was a significant risk in our cohort (Table 2).

Although phacoemulsification has often been performed in combination with 25 G sutureless PPV with a relatively favorable safety profile, we found limited evidence addressing the incidence of post-PPV endophthalmitis after PPV is performed in combination with cataract surgery.^{15,16,20} A study by Chen et al reported one case of postoperative endophthalmitis among 46 cases (rate of 2.17%) undergoing combined 25 G PPV and CE. In their study, subconjunctival injections of antibiotics at the conclusion of surgery were administered at the surgeon's discretion.¹⁵ A study by Wani et al reported three cases of postoperative endophthalmitis after 401 cases of combined 25 G PPV and CE (rate of 0.75%), whereas the incidence of endophthalmitis in isolated 25 G PPV alone was 1.2 per 1,000 cases; 0.12% (3 out of 2,564 cases). Prophylactic subconjunctival antibiotics were used routinely in their study.¹⁶ The numbers of cases in both studies were relatively small as they sought to determine the incidence of postoperative endophthalmitis after combined 25 G PPV and CE. However, both groups reported incidence of endophthalmitis after combined 25 G PPV and CE that was higher than the known endophthalmitis rate after isolated PPV, despite the use of prophylactic subconjunctival antibiotics in their cohort. Although the numbers of cases are limited in these studies, the incidence of endophthalmitis after PPV combined with anterior segment procedures with or without prophylactic subconjunctival antibiotics was similar to our findings.

As cataract progression may occur in up to 80% of patients after vitrectomy, the combination procedure may be beneficial in patients with a visually significant cataract and vitreoretinal pathology. In the United States, combined surgery seems to be performed less commonly than are isolated PPV procedures. Reasons for this include the availability of two surgeons, the preparation of two different operative systems, or no immediate indication for combined surgery. Nevertheless, previous reports and data from this study indicate that caution is needed in selecting patients for combined PPV and anterior segment procedures. The cause of the higher rate of postoperative endophthalmitis after combined transconjunctival PPV and CE is unclear, and may be out of the scope of this study. Further studies will be necessary to determine the recommended prophylactic practice to prevent postoperative endophthalmitis after combined PPV and CE.

Aside from the questionable role of prophylactic subconjunctival antibiotics in preventing postoperative endophthalmitis after PPV, several other disadvantages must be considered. Anaphylaxis and globe perforation after subconjunctival injection of antibiotics have been reported.²¹⁻²³ An increase in the numbers of multidrug-resistant organisms is a serious concern, and the Centers for Disease Control and Prevention (CDC) warns that vancomycin should not be used as a prophylactic antibiotic.^{24,25} Extra costs are also involved because the procedures are performed \sim 250,000 times per year in the United States and \sim 500,000 times per year worldwide.¹² Approximately \$2.5 to 5.0 million from the cost of medication and the handling fee could be saved per year in the United States.

Our study had several limitations. The retrospective noncomparative nature of the study does not permit us to confirm that prophylactic subconjunctival antibiotics are ineffective in preventing post-PPV endophthalmitis. The small number of endophthalmitis cases may not allow us to examine all risk factors in postoperative endophthalmitis when no prophylactic subconjunctival antibiotics are applied. However, our study benefits from our more than six years of clinical experience in performing transconjunctival PPV without prophylactic subconjunctival antibiotics, with a rate of postoperative endophthalmitis similar to that of previous reports.

In conclusion, this retrospective study demonstrated that performing transconjunctival PPV without prophylactic subconjunctival antibiotics did not lead to an increase in incidence of postoperative endophthalmitis. The data from this study support the practice of not using prophylactic subconjunctival antibiotics after transconjunctival PPV. Additional studies are needed to reduce the postoperative endophthalmitis after transconjunctival PPV combined anterior segment procedures.

Key words: post-PPV endophthalmitis, prophylactic subconjunctival antibiotics.

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