

Role of intracameral antibiotics in endophthalmitis prophylaxis following-cataract surgery

Post-cataract surgery endophthalmitis is a rare complication with an incidence of 0.03–0.2%.^[1] The prognosis is usually guarded and results in a loss of visual acuity as well as the anatomical integrity of the eye in severe cases.

Various factors contribute to the development of postoperative endophthalmitis, including use of contaminated surgical instruments or irrigating fluids, complicated cataract surgery, intraocular contamination by indigenous flora, wound leak, postoperative transient hypotony resulting in wound gape and the influx of surface fluid, immunocompromised host status or local lid, and ocular surface anomalies.^[2,3] Good surgical asepsis is the cornerstone to prevent postsurgical infections, and various preoperative, intraoperative, and postoperative measures have been proposed to decrease the incidence of endophthalmitis after cataract surgery. The rationale for use of these perioperative asepsis measures in cataract surgery is based on a reduction of the ocular surface and periocular flora which may potentially result in intraocular contamination. A high bacterial contamination rate of up to 46.25% has been observed in aqueous samples obtained at the end of phacoemulsification, with coagulase-negative *Staphylococcus* being the most common species isolated.^[4] Baillif *et al.* observed anterior chamber bacterial contamination in only 1.8% cases after using povidone-iodine 10% and 5% to decontaminate the periocular skin and ocular surface respectively, in conjunction with a single dose of oral ofloxacin 400 mg administered 2 h before surgery.^[5] Sobaci *et al.* observed a more than the threefold decrease in bacterial contamination of the aqueous samples obtained after phacoemulsification with the use of antibiotic-containing irrigating solutions.^[6] Bacterial growth was observed in aqueous samples of 21.1% cases wherein antibiotic-infused irrigating solutions were not used, compared with 6.8% in cases performed using antibiotic-infused irrigating solutions.

A survey of endophthalmitis prophylaxis measures among 800 surgeons in the United Kingdom revealed the routine use of preoperative topical antibiotics by 5.9% surgeons, use of 10% povidone-iodine for cleaning the periocular skin by 99.4%, instillation of povidone-iodine in the conjunctival sac by 69.8%, intracameral antibiotic usage by 13.6%, subconjunctival antibiotics by 77.3%, and postoperative antibiotics by more than 90% surgeons.^[7] In 2007, the European Society of Cataract and Refractive Surgeons (ESCRS) conducted the first randomized controlled trial and observed a five-fold decrease in the incidence of postsurgical endophthalmitis with the use of intracameral cefuroxime.^[8] This led to increased adoption of the routine use of intracameral antibiotics as prophylaxis from 30% in 2007 to nearly 50% in 2014.^[9,10] However; there is a lack of conclusive evidence establishing the use of intracameral antibiotics as the definitive standard of care, and asepsis practices generally vary from surgeon to surgeon.

Preoperative measures

A comprehensive preoperative evaluation is essential to identify patients at high risk for developing postsurgical endophthalmitis, and optimization of systemic status, as well as treatment of localized lid and ocular surface disorders, is imperative before undertaking cataract surgery. Povidone-iodine is routinely used in the immediate preoperative period with a 10% solution to clean the periocular skin and a 5% solution instilled in the conjunctival sac. It results in a significant decrease in the pathogenic bacterial load during and immediately after the surgery; however, it does not alter the growth pattern and antibiotic susceptibility of the native conjunctival flora and thus prevents the emergence of drug resistance.^[11–13] A contact time of at least 30 s is recommended to reduce the bacterial colony-forming units on the ocular surface.^[14] The use of povidone-iodine may be associated with adverse effects such as edema of epithelial cells, endothelial toxicity, and iridocyclitis.^[15] Sterile speculum and surgical drapes to isolate the eyelashes from the surgical field and the use of topical antibiotics in the perioperative period are also routinely practiced. Fluoroquinolones are preferred for topical use and instilled 0–3 days before surgery. The use of topical antibiotics in the preoperative period is not associated with a significant decrease in the rates of postsurgical endophthalmitis. Moreover, prophylactic antibiotic use is linked to the emergence of drug resistance.^[16,17] Trimming of eyelashes in the preoperative period is no longer advocated as it does not lead to a decrease in the incidence of postsurgical endophthalmitis and distorts the cosmetic appearance of the patient.

Intraoperative measures

The main pathogenic mechanism of post-cataract surgery endophthalmitis is related to intraocular contamination by indigenous surface flora during and immediately after surgery, and intraocular instillation of antibiotics during surgery is increasingly being adopted by surgeons as an effective modality to prevent endophthalmitis. Srinivasan *et al.* observed that the addition of vancomycin to irrigating solutions used intraoperatively was significantly more efficacious in reducing aqueous contamination as compared with preoperative topical antibiotic usage.^[18] Haripriya *et al.* observed a 3.5 times reduction in endophthalmitis rates with the use of intracameral moxifloxacin as prophylaxis after cataract surgery.^[19] In addition, they observed a significant benefit in cases with complicated cataract surgery and posterior capsular rupture, wherein the endophthalmitis rates decreased from 0.48% to 0.21% with the use of intracameral moxifloxacin.

Intraoperatively, antibiotics may be instilled in the irrigating solution, injected as a bolus either intracamerally or subconjunctivally toward the end of surgery or instilled topically on the ocular surface after hydrating the corneal incisions. Present-day micro-incision cataract surgery is often performed under topical anesthesia rather than peri-bulbar blocks, and this has led to a shift in surgeon preference from using subconjunctival antibiotic injections to instillation of intracameral antibiotics. The use of antibiotics in irrigating solutions is associated with difficulty in monitoring the intraocular concentrations of antibiotics with a wide variability as well as an increased potential risk of endothelial and macular

toxicity, especially with aminoglycosides like gentamicin and amikacin.

Intracameral injection of antibiotics has emerged as the preferred modality of intraoperative antibiotic use during cataract surgery. At present, various antibiotics are routinely used intracamerally, including cefuroxime, vancomycin, and moxifloxacin. These may be administered in the bag behind the intraocular lens toward the end of the surgery, instilled in the anterior chamber or instilled at wound-site. The routinely used intracameral dosage is 1 mg/0.1 mL for cefuroxime and vancomycin, and 0.5 mg/0.1 mL for moxifloxacin.

However, various safety and logistical concerns surround the routine use of intracameral antibiotics. First, there are few commercial formulations of cefuroxime (Aprokam, Thea Pharmaceuticals, Newcastle Under Lyme, UK) and moxifloxacin (Auromox, Aurolab, Madurai, India, and 4-Quin PFS 0.5% single-use prefilled syringes) for intraocular use, which are not widely available and not approved by the United States FDA. A commercial preparation of self-preserved moxifloxacin eyedrops (Vigamox 0.5% ophthalmic solution) has also been reported to be safe and efficacious for intracameral use.^[20,21]

Second, the use of intracameral antibiotics may in itself be associated with adverse drug reactions. Intracameral cefuroxime use is associated with uveitis, retinal infarction, and macular edema. Endothelial cell loss and toxicity may occur, and toxic anterior segment syndrome, as well as anaphylactic reactions, have been reported after the use of intracameral antibiotics. Hemorrhagic occlusive retinal vasculitis has been reported exclusively after the use of intracameral vancomycin.^[20,21]

Both cefuroxime and vancomycin are mainly active against Gram-positive organisms and do not provide coverage against Gram-negative organisms. Moxifloxacin has a relatively

broader spectrum and covers both Gram-positive and Gram-negative organisms. Intracameral cefuroxime has a time-dependent action and the aqueous concentration is above the minimum inhibitory concentration (MIC) for 4–5 h, which limits its usefulness in the postoperative period. Moxifloxacin has a dose-dependent action and achieves an initial aqueous concentration up to 300 times greater than the MIC when injected intracamerally in a dose of 0.5 mg/0.1 mL.^[20-22] It maintains its efficacy for a longer duration as compared with cefuroxime.

Drug resistance, though uncommon, has been observed after the use of intracameral antibiotics. Increased resistance of coagulase-negative *Staphylococcus* species has been observed to fluoroquinolones, including moxifloxacin, with a decrease in susceptibility from 77% to 43% since 2004.^[23] An increased incidence of enterococci endophthalmitis and fungal endophthalmitis has been observed in cases receiving intracameral cefuroxime. Moreover, the prognosis of postsurgical endophthalmitis in cases that received intracameral cefuroxime is dismal. The standard intravitreal drugs may not be effective in these cases with drug-resistant endophthalmitis, and a combination of newer generation antibiotics may often be needed to salvage the eye.

There is only one randomized controlled trial (ESCRS study) that observed the definitive role of intracameral cefuroxime in reducing the incidence of endophthalmitis.^[8] There is a lack of level I evidence for the use of intracameral vancomycin and moxifloxacin. The majority of studies are retrospective in nature and generally compare the incidence of endophthalmitis before and after the institution of intracameral antibiotics [Table 1].^[19-21,24-28]

The present study observed similar endophthalmitis rates between the two groups using intracameral cefuroxime and moxifloxacin. They observed a decrease in the rates of endophthalmitis with the usage of intracameral antibiotics;

Table 1: Evidence for intracameral antibiotic use for post-cataract surgery endophthalmitis prophylaxis

Study (Year)	Study Design	Sample Size	Antibiotic	Results
ESCRS endophthalmitis study group (2007) ^[8]	Randomized controlled trial	16603	Cefuroxime	Endophthalmitis rate: 0.6 per 1000 surgeries with intracameral cefuroxime versus 3.0 per 1000 surgeries without intracameral cefuroxime
Jabbarvand <i>et al.</i> (Ophthalmology 2016) ^[24]	Retrospective	480,104	Cefuroxime	No cases of endophthalmitis were observed among the 25,920 patients who received intracameral cefuroxime
Daien <i>et al.</i> (JAMA Ophthalmology 2017) ^[25]	Retrospective	3,351,401	Cefuroxime	Decreased incidence of postoperative endophthalmitis as the use of cefuroxime prophylactic injections increased No increased risk of retinal cystoid macular edema
Creuzot-Garcher <i>et al.</i> (Ophthalmology 2016) ^[26]	Retrospective	6,371,242	Not specified	Intracameral antibiotic injection was associated with a lower risk of acute postoperative endophthalmitis
Au <i>et al.</i> (Clin Exp Ophthalmol 2016) ^[27]	Retrospective longitudinal cohort study	14805	Vancomycin	9-fold reduction in the rate of acute postoperative endophthalmitis
HariPriya <i>et al.</i> (Ophthalmology, 2016) ^[28]	Retrospective clinical registry	116,714	Moxifloxacin	4-fold reduction in postoperative endophthalmitis in patients undergoing M-SICS with intracameral moxifloxacin use
HariPriya <i>et al.</i> (Ophthalmology 2017) ^[19]	Retrospective clinical registry	617,453	Moxifloxacin	3.5-fold reduction in endophthalmitis rates with intracameral moxifloxacin (3-fold for M-SICS and nearly 6-fold for phacoemulsification).

however, they performed a retrospective comparison between the cohort of cases receiving intracameral antibiotics to cases performed before the routine use of intracameral antibiotics in their centers. The majority of the surgeries were small-incision cataract surgery (SICS).^[29]

Postoperative measures

Topical antibiotics should be instituted within 4–6 h of surgery when the efficacy of intracameral or subconjunctival antibiotics starts decreasing. Fluoroquinolones are the preferred antibiotics for postoperative use, and they are routinely instilled by a majority of surgeons till 1–4 weeks. There is no definitive evidence that their usage prevents postsurgical endophthalmitis. Topical antibiotics should not be tapered to prevent the emergence of drug resistance. There is no role of systemic antibiotics in preventing postsurgical endophthalmitis.

Conclusion

The reduction in postsurgical endophthalmitis over the decades may be attributed to the increasing emphasis on good surgical asepsis as well as the routine use of povidone-iodine for periocular cleaning, sterile surgical drapes, and speculums. An improvement in sterilization techniques along with the increasing use of disposable surgical instruments, tubings, and cassettes has also reduced the risk of contamination and resulted in a decrease in the incidence of endophthalmitis.

In the present-day scenario, the role of intracameral antibiotics remains controversial, with a paucity of level I evidence to definitively establish its benefit. The large-scale retrospective analysis points toward a significant beneficial trend of using intracameral antibiotics for endophthalmitis prophylaxis, which has led to the adoption of their routine usage as a preferred practice for many surgeons and institutions worldwide. In addition, a systematic review of 18 studies including one randomized controlled trial observed consistent evidence in support of the use of intracameral cefuroxime to decrease the incidence of post-cataract surgery endophthalmitis.^[30] Commercial drug preparations for intracameral use may not be universally available and are not approved by the drug regulatory authorities. There is a risk of toxic adverse effects from the use of intracameral antibiotics itself. In addition, there are concerns about antibiotic resistance due to their widespread usage. There is a debate regarding the cost-effectiveness of routine intracameral antibiotic prophylaxis; however, in our view, the risk of developing a potentially sight-threatening disease such as endophthalmitis far outweighs the economic consideration of routine antibiotic usage.

Perioperative prophylactic measures against infection are mandatory in any surgical procedure, and the choice of antibiotic prophylaxis may be governed by a variety of factors including availability of commercial preparations of the drug, approval of the method by drug regulatory bodies, adverse effects, surgeon preference, and the risk-benefit ratio. With increasing preference for topical anesthesia during phacoemulsification, intracameral instillation of antibiotics appears to be a safe and effective method to prevent post-cataract endophthalmitis. In the absence of definitive evidence against the beneficial effect of intracameral antibiotics, they may be routinely administered as prophylaxis post-cataract surgery.

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References

- Vaziri K, Schwartz SG, Kishor K, Flynn HW Jr. Endophthalmitis: State of the art. *Clin Ophthalmol* 2015;9:95-108.
- McDonnell PJ, Taban M, Sarayba M, Rao B, Zhang J, Schiffman R, *et al.* Dynamic morphology of clear corneal cataract incisions. *Ophthalmology* 2003;110:2342-8.
- Herretes S, Stark WJ, Pirouzmanesh A, Reyes JM, McDonnell PJ, Behrens A. Inflow of ocular surface fluid into the anterior chamber after phacoemulsification through sutureless corneal cataract wounds. *Am J Ophthalmol* 2005;140:737-40.
- Srinivasan R, Tiroumal S, Kanungo R, Natarajan MK. Microbial contamination of the anterior chamber during phacoemulsification. *J Cataract Refract Surg* 2002;28:2173-6.
- Baillif S, Roure-Sobas C, Le-Duff F, Kodjikian L. Aqueous humor contamination during phacoemulsification in a university teaching hospital. *J Fr Ophthalmol* 2012;35:153-6.
- Sobaci G, Tuncer K, Taş A, Ozyurt M, Bayer A, Kutlu U. The effect of intraoperative antibiotics in irrigating solutions on aqueous humor contamination and endophthalmitis after phacoemulsification surgery. *Eur J Ophthalmol* 2003;13:773-8.
- Gordon-Bennett P, Karas A, Flanagan D, Stephenson C, Hingorani M. A survey of measures used for the prevention of postoperative endophthalmitis after cataract surgery in the United Kingdom. *Eye (Lond)* 2008;22:620-7.
- Endophthalmitis Study Group, European Society of Cataract and Refractive Surgeons. Prophylaxis of postoperative endophthalmitis following cataract surgery: Results of the ESCRS multicenter study and identification of risk factors. *J Cataract Refract Surg* 2007;33:978-88.
- Chang DF, Braga-Mele R, Henderson BA, Mamalis N, Vasavada A; ASCRS Cataract Clinical Committee. Antibiotic prophylaxis of postoperative endophthalmitis after cataract surgery: Results of the 2014 ASCRS member survey. *J Cataract Refract Surg* 2015;41:1300-5.
- Chang DF, Braga-Mele R, Mamalis N, Masket S, Miller KM, Nichamin LD, *et al.* Prophylaxis of postoperative endophthalmitis after cataract surgery: Results of the 2007 ASCRS member survey. *J Cataract Refract Surg* 2007;33:1801-5.
- Ahmed Y, Scott IU, Pathengay A, Bawdekar A, Flynn HW Jr. Povidone-iodine for endophthalmitis prophylaxis. *Am J Ophthalmol* 2014;157:503-4.
- Ciulla TA, Starr MB, Masket S. Bacterial endophthalmitis prophylaxis for cataract surgery: An evidence-based update. *Ophthalmology* 2002;109:13-24.
- Wu PC, Li M, Chang SJ, Teng MC, Yow SG, Shin SJ, *et al.* Risk of endophthalmitis after cataract surgery using different protocols for povidone-iodine preoperative disinfection. *J Ocul Pharmacol Ther* 2006;22:54-61.
- Friedman DA, Mason JO, Emond T, McGwin G. Povidone iodine contact time and lid speculum use during intravitreal injection. *Retina* 2013;33:975-81.
- Jiang J, Wu M, Shen T. The toxic effect of different concentrations of povidone iodine on the rabbit's cornea. *Cutan Ocul Toxicol* 2009;28:119-24.
- Chen RW, Rachitskaya A, Scott IU, Flynn HW Jr. Is the use of topical antibiotics for intravitreal injections the standard of care or are we better off without antibiotics? *JAMA Ophthalmol* 2013;131:840-2.

17. Bhavsar AR, Stockdale CR, Ferris FL III, Brucker AJ, Bressler NM, Glassman AR; for the Diabetic Retinopathy Clinical Research. Update on risk of endophthalmitis after intravitreal drug injections and potential impact of elimination of topical antibiotics. *Arch Ophthalmol* 2012;130:809-10.
18. Srinivasan R, Gupta A, Kaliaperumal S, Babu RK, Thimmarayan SK, Belgode HN. Efficacy of intraoperative vancomycin in irrigating solutions on aqueous contamination during phacoemulsification. *Indian J Ophthalmol* 2008;56:399-402.
19. Haripriya A, Chang DF, Ravindran RD. Endophthalmitis reduction with intracameral moxifloxacin prophylaxis: Analysis of 600 000 surgeries. *Ophthalmology* 2017;124:768-75.
20. Braga-Mele R, Chang DF, Henderson BA, Mamalis N, Talley-Rostov A, Vasavada A; ASCRS Clinical Cataract Committee. Intracameral antibiotics: Safety, efficacy, and preparation. *J Cataract Refract Surg* 2014;40:2134-42.
21. Haripriya A. Antibiotic prophylaxis in cataract surgery – An evidence-based approach. *Indian J Ophthalmol* 2017;65:1390-5.
22. George NK, Stewart MW. The routine use of intracameral antibiotics to prevent endophthalmitis after cataract surgery: How good is the evidence? *Ophthalmol Ther* 2018;7:233-45.
23. Stringham JD, Relhan N, Miller D, Flynn HW Jr. Trends in fluoroquinolone nonsusceptibility among coagulase-negative Staphylococcus isolates causing endophthalmitis, 1995-2016. *JAMA Ophthalmol* 2017;135:814-5.
24. Jabbarvand M, Hashemian H, Khodaparast M, Jouhari M, Tabatabaei A, Rezaei S. Endophthalmitis occurring after cataract surgery: Outcomes of more than 480 000 cataract surgeries, epidemiologic features, and risk factors. *Ophthalmology* 2016;123:295-301.
25. Daien V, Papinaud L, Gillies MC, Domerg C, Nagot N, Lacombe S, *et al.* Effectiveness and safety of an intracameral injection of cefuroxime for the prevention of endophthalmitis after cataract surgery with or without perioperative capsular rupture. *JAMA Ophthalmol* 2016;134:810-6.
26. Creuzot-Garcher C, Benzenine E, Mariet AS, de Lazzar A, Chiquet C, Bron AM, *et al.* Incidence of acute postoperative endophthalmitis after cataract surgery: A nationwide study in France from 2005 to 2014. *Ophthalmology* 2016;123:1414-20.
27. Au CP, White AJ, Healey PR. Efficacy and cost-effectiveness of intracameral vancomycin in reducing postoperative endophthalmitis incidence in Australia. *Clin Exp Ophthalmol* 2016;44:803-11.
28. Haripriya A, Chang DF, Namburur S, Smita A, Ravindran RD. Efficacy of intracameral moxifloxacin endophthalmitis prophylaxis at Aravind Eye Hospital. *Ophthalmology* 2016;123:302-8.
29. Rathi VM, Sharma S, Das T, Khanna RC. Endophthalmitis prophylaxis study. Report 1: Intracameral cefuroxime and moxifloxacin prophylaxis for the prevention of postcataract endophthalmitis in rural India. *Indian J Ophthalmol* 2020;68:819-24.
30. Kessel L, Flesner P, Andresen J, Erngaard D, Tendal B, Hjortdal J. Antibiotic prevention of postcataract endophthalmitis: A systematic review and meta-analysis. *Acta Ophthalmol* 2015;93:303-17.

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