Endophthalmitis Prophylaxis Study, Report 2: Intracameral antibiotic prophylaxis with or without postoperative topical antibiotic in cataract surgery

Varsha M Rathi, Savitri Sharma¹, Taraprasad Das², Rohit C Khanna

Purpose: Intracameral antibiotic in cataract surgery has shown level I evidence as prophylaxis for postoperative endophthalmitis. Not much is known if one should also use topical antibiotics after intracameral injection. The purpose of the study was to determine efficacy of intracameral antibiotic with and without postoperative topical antibiotic in reducing the incidence of acute endophthalmitis after cataract surgery in rural India. Methods: A prospective comparative, non-randomized interventional study was designed in 15 rural centres in India. The study recruited 40,006 patients (n = 42,466 eyes), who underwent cataract surgery (phacoemulsification/small incision cataract surgery), and received intracameral antibiotic (cefuroxime/moxifloxacin). Postoperative topical antibiotic prescription was left to the choice of the treating physician, but they were encouraged not to use it in uneventful surgeries. Primary outcome measure was occurrence of acute clinical endophthalmitis within 6 weeks of surgery. Statistical analysis was done using STATA software v13.1 (StataCorp, Texas); P value of <0.05 was considered statistically significant. Results: In the study, 17,932 (42%) eyes received intracameral cefuroxime (ICC) and 24,534 (58%) eyes received intracameral moxifloxacin (ICM). Topical antibiotic was not prescribed to 17,855 (42%) eyes - 5723 (32%) eyes in ICC group and 12,132 (68%) eyes in ICM group. Acute clinical endophthalmitis occurred in 15 (0.035%) eyes - 1 / 3515 (0.028%) eyes and 1 / 2231 (0.045%) eyes that received and did not receive topical antibiotic, respectively. The difference in occurrence of endophthalmitis with/without topical antibiotics in each group (ICC: 0.016% and 0.017%; P = 0.958; ICM: 0.040% and 0.058%; P = 0.538) was not significant (P = 0.376). Conclusion: Supplementing intracameral antibiotic with topical antibiotic postoperatively did not impact the occurrence of acute post cataract surgery endophthalmitis in rural India.

Key words: Cataract surgery, Intracameral cefuroxime, intracameral moxifloxacin, postoperative no topical antibiotics, postoperative topical antibiotics

Post-cataract surgery endophthalmitis, though rare, often results in poor visual and anatomical outcome. Evidence-based prophylaxis for prevention includes preoperative preparation of the eye and skin around the eye, preventing eyelash exposure in the field of surgery, and using intracameral antibiotics.[1-4] There are reports of significant reduction in post-cataract surgery endophthalmitis with the use of both intracameral cefuroxime and moxifloxacin.[4-7] Most of the infections occur due to intraoperative inoculation of the organisms. Currently, perioperative systemic antibiotic is not a standard of care and preoperative topical antibiotics are not routinely used.[8-11] Surgeons are increasingly using intracameral antibiotics in presence of intraocular complications such as zonular dehiscence and posterior capsular rent.[12-14] While postoperative topical antibiotics after frequent administrations can attain adequate minimum inhibitory concentration levels in the anterior chamber, the prophylactic value of topical antibiotics, invariably started after 24 hours of surgery, is questionable. Thus eradication of the pathogens before they gain entry into the eye from the ocular surface is crucial.[13]

The Endophthalmitis Prophylaxis Study (EPS) was designed to prospectively compare the efficacy of intracameral cefuroxime (ICC) and intracameral moxifloxacin (ICM) in reducing the incidence of acute endophthalmitis after cataract surgery (primary aim; EPS#1).[10] Intracameral cefuroxime and moxifloxacin, with proven safety and efficacy, were used in the study.[4,12,13] The secondary aim of the EPS was to look at the incidence of endophthalmitis with and without topical antibiotics after intracameral antibiotic. The current study (EPS#2) analyzed the eyes that received intracameral antibiotic but did not receive postoperative topical antibiotic.

Methods

The EPS was approved by the Institutional Review Board (IRB)/Ethics Committee (LEC 08-16-066) and the described research adhered to the tenets of the Declaration of Helsinki. The study population and methodology is already described.[10] In brief, the study included patients who underwent cataract surgery due to cataract in rural areas in India, and were randomized to receive either intracameral cefuroxime (ICC) or intracameral moxifloxacin (ICM) along with routine postoperative topical antibiotic. The study was designed as a prospective, comparative, non-randomized intervention study, powered to detect a 5% incidence of endophthalmitis in each arm, assuming a 2% incidence of endophthalmitis in the control arm. The study population consisted of 40,006 patients (n = 42,466 eyes), who underwent cataract surgery (phacoemulsification/small incision cataract surgery), and received intracameral antibiotic (cefuroxime/moxifloxacin).

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

Cite this article as: Rathi VM, Sharma S, Das T, Khanna RC. Endophthalmitis Prophylaxis Study, Report 2: Intracameral antibiotic prophylaxis with or without postoperative topical antibiotic in cataract surgery. Indian J Ophthalmol 2020;68:2451-5.

Allen Foster Research Centre for Community Eye Health, Gullapalli Pratibha Rao International Centre for Advancement of Rural Eye Care, L V Prasad Eye Institute (LVPEI), Banjara Hills, Hyderabad; Jhaveri Microbiology Centre, Biren Holden Eye Research Centre, LVPEI, Hyderabad; Kanuri Santhamma Centre for Vitreoretinal Diseases, LVPEI, Hyderabad, India

Correspondence to: Dr. Rohit C Khanna, L V Prasad Eye Institute, Hyderabad - 500 034, Telangana, India. E-mail: rohit@lvpei.org

Received: 24-Sep-2019 Revision: 13-Dec-2019 Accepted: 21-May-2020 Published: 26-Oct-2020

© 2020 Indian Journal of Ophthalmology | Published by Wolters Kluwer - Medknow
surgery between October 2016 and March 2018 in 15 rural eye centres network in India. The centres, selected based on the distance from the eye institute to the referral tertiary centres (up to 350 km and/or 2-8 hours of journey), were divided into two groups—one group to use ICC and the other to use ICM. All patients provided informed consent. Patients above 18 years of age and who underwent surgeries either by phacoemulsification or manual small incision cataract surgery (SICS) were included. Patients who underwent cataract surgery combined with any other intraocular procedures, planned intra-capsular (ICCE) or extra-capsular (ECCE) cataract extraction, were excluded. All eyes were prepared with application of povidone iodine (5% for conjunctiva and 10% for the skin). Hydroxy propyl methyl cellulose was the viscoelastic used in all eyes. All patients received intracameral antibiotic, preselected for ICC or ICM (described in EPS # 1).19] Following surgery, all patients received topical corticosteroid (1% prednisolone acetate), and the decision to prescribe topical antibiotic was left to the discretion of the operating surgeons. In general, the operating surgeon did not prescribe postoperative topical antibiotic to people with good ocular hygiene (preoperatively absence of grade 3 meibomitis and/or blepharitis) and in eyes that had no intra-operative complications. When antibiotic was prescribed, it was a fluoroquinolones, such as moxifloxacin (Sun Pharmaceuticals Ind. Ltd, Halol, India) or ciprofloxacin (Cipla Ltd, Mumbai, India) or ofloxacin (Allergan Pharmaceuticals, Westport, Ireland), applied 4 times daily for a week. The data collected from patients who developed clinical acute endophthalmitis within 6 weeks post surgery was analysed.

All patients were examined on postoperative day one, between days 4-10 and between weeks 3-11. The follow-up examination included recording the uncorrected visual acuity (UCVA), refraction vision at or after 3-week visit, slit-lamp examination, Goldman applanation tonometry and fundoscopy. The diagnosis of endophthalmitis was based on the clinical findings, such as reduction or no improvement in vision, congestion of the eye, anterior chamber cells/flare and/or hypopyon, vitreous exudates visible through indirect ophthalmoscopy or detected by B-scan ultrasonography, and the clinical judgment of the treating surgeon. The diagnosis was confirmed by one of the authors (VMR) through tele-consultation as well as the retina surgeon in the referral hospital and subsequently, after referral the case was seen and confirmed by a retina specialist as well as Hospital Infection Control Committee. Appropriate treatment was instituted to all the people.

Treatment in the rural centre consisted of intravitreal antibiotics injection (ceftazidime 2.25 mg in 0.1 ml, and vancomycin 1.0 mg in 0.1 ml); topical cycloplegic and intensive topical fluoroquinolone and corticosteroid (Prednisolone acetate 1%), recommended by the Endophthalmitis Vitrectomy Study (EVIS).[27] About 0.3-0.5 ml of vitreous was aspirated manually from the mid vitreous cavity using a 23 g needle mounted on a 2 ml syringe before intravitreal antibiotics were injected. These patients were referred to the nearest tertiary eye centres (up to 350 kms and/or 2-8 hours journey). Further treatment at the tertiary centres was under the care of retina specialists and consisted of either close observation or repeat intraocular antibiotics (with/without intravitreal dexamethasone) and with/without vitrectomy. In an event of surgical intervention, the vitrectomy aspirate was sent for microbiological evaluation (microscopy, culture, and polymerase chain reaction test for bacteria and fungi).

Statistical analysis
Baseline characteristic difference between the groups using topical antibiotic versus not using topical antibiotic was tested using chi square test. Risk factor analysis was done using logistic regression. Statistical analysis was done using STATA software version 13.1 (StataCorp, Texas). A P value of <0.05 was considered as statistically significant.

Results
A total of 42,582 surgeries were performed during the 18-month study period (October 2016 to March 2018) at 15 rural centres. The rural centres, located in large villages or small towns, offer comprehensive eye care with a focus on cataract surgery and correction of uncorrected refractive error. All economically underprivileged patients were operated at no cost to them. Of the total surgeries, 116 eyes were excluded as these were either combined with glaucoma surgeries, or operated by techniques other than SICs or phacoemulsification (such as ICCE and ECCE). The current analysis included 42,466 cataract surgeries [40,006 persons; Male-18,350 (45.9%); no-cost to patient - 29,895 (70.4%)]. The SICS technique was used in 36,414 (85.7%) eyes and phacoemulsification technique was used in 6,052 (14.3%) eyes. Table 1 shows the baseline demographics and ocular characteristics in two groups of eyes that either received or did not receive topical antibiotics postoperatively. Intracameral antibiotic was injected in all these patients - cefuroxime in 17,932 (42.2%) eyes and moxifloxacin in 24,534 (57.8%) eyes. Post-operative topical antibiotic was given to a significant number of people who were operated at no cost to them; n = 17,157 (69.71%); to more number of eyes operated by the SICS technique, n = 20,807 (84.54%); and to people operated by the ophthalmology fellows, n = 17,321 (70.38%) and trainees, n = 1844 (7.49%).

Postoperative topical antibiotic was prescribed to 24,611 (58%) eyes, almost equally divided between the ICC (12,209 eyes) and ICM (12,402 eyes) groups and included 986 eyes with intraoperative complications. Postoperative topical antibiotic was not prescribed in 17,885 (42%) eyes - less often in the ICC group (5,723 eyes) than the ICM group (12,132 eyes). The endophthalmitis occurred in 0.028% in the eyes receiving topical antibiotic (1 per 3515 operated eyes) and 0.045% in the eyes not receiving topical antibiotic (1 per 2231 operated eyes that did not receive topical antibiotic). This was not statistically significant (P = 0.376) [Fig. 1]. Similarly, in the ICM group, there was no statistically significant difference in the rate of endophthalmitis with topical antibiotics (0.016% - 1 case in 6104 operated eyes) or without topical antibiotic (0.017% - 1 case in 5723 operated eyes), (P = 0.958). Likewise, in the ICM group, there was no statistically significant difference in the rate of endophthalmitis with topical antibiotics (0.04% - 1 case in 2480 operated eyes) or without topical antibiotic (0.058% - 1 case in 1733 operated eyes), (P = 0.538).

The distribution of postoperative topical antibiotic (n = 24,611 eyes) was as follows: ciprofloxacin 18,091 (73.5%) eyes, ofloxacin 3,298 (13.4%) eyes, and moxifloxacin 3,222 (13.1%) eyes. Seven eyes developed acute endophthalmitis in the topical antibiotic group – six eyes where topical ciprofloxacin was used, one eye where ofloxacin was used, and none where moxifloxacin was used. There was no statistical significance attached to any topical antibiotic [Table 2].

Table 3 shows the occurrence of endophthalmitis with and without topical antibiotics after phacoemulsification and SICS surgeries. There was no significant association in the occurrence of endophthalmitis with the use of any of the specific topical antibiotic in phacoemulsification and SICS surgeries group.

In terms of risk factors for endophthalmitis, none of the factors (age, gender, paying status, surgeon, surgical technique, and type of intraocular antibiotic and use or no use of topical antibiotics in the postoperative period) were significant upon both uni- and multi-variate regression analysis (data not shown).
The profile of the 15 cases of endophthalmitis including one case of panophthalmitis was as follows: Intracameral antibiotics with postoperative topical antibiotics - 7, of which 3 (42.8%) were culture positive; intracameral antibiotics without postoperative topical antibiotics - 8, of which 4 (50%) were culture positive. Culture positive cases included 1 fungal and 6 bacterial infections. The details of microbiological analysis would be shared in subsequent publications.

**Discussion**

Studies have shown that intracameral cefuroxime and moxifloxacin are known to reduce the incidence of post cataract surgery acute endophthalmitis, and that postoperative topical antibiotic may not be mandatory. The current study shows that deletion of postoperative topical antibiotic does not impact the rate of postoperative acute endophthalmitis, and is independent of the choice of intracameral antibiotic (cefuroxime and moxifloxacin) and topical antibiotic (one of the fluoroquinolones).

Based on the study results, we estimated the economic benefit of confining to intracameral antibiotic and eliminating postoperative topical antibiotic in India. The basis of the calculation was based on the following facts: (1) The rate of post cataract surgery acute endophthalmitis is 0.035% after intracameral antibiotic (our results in EPS # 1); (2) Rate of endophthalmitis with intracameral with topical antibiotic is 0.028% and intracameral antibiotic without topical antibiotic is 0.045% (current study), and (3) 6.481 million cataract surgeries were performed in the year 2016-17 in India. In our earlier study, we reported an annual savings of INR 6-130 million.
because of managing reduced number of endophthalmitis after intracameral antibiotic. The cost of cataract surgery care could be further reduced by INR 110-758 million by eliminating topical ciprofloxacin and moxifloxacin, respectively, once intracameral antibiotic becomes the standard of care in India [Table 4].

With the availability of newer fluoroquinolones, we expect that many practicing ophthalmologists would be using higher fluoroquinolone, such as moxifloxacin and gatifloxacin (3rd generation quinolone). The practice of topical ciprofloxacin (2nd generation quinolone) in our rural centres must have been influenced by the lower prices in India (cheapest fluoroquinolone), by the large “no-cost-to-patient” surgery volume (70.4% in this series), and our earlier publication that the efficacy of ciprofloxacin is not inferior to other quinolone antibiotics.

The limitations of the study include non-randomization and the decision to using topical antibiotic being left to the discretion of the treating physician.

**Conclusion**

In conclusion, this non-randomized study showed that there was no significant difference in the occurrence of endophthalmitis with or without postoperative topical antibiotics after intracameral antibiotic in uneventful cataract surgeries. This needs to be further evaluated in a randomized study. This, however, does not rule out the other standard procedures mandatory - preoperative preparation and intraoperative care.

**Acknowledgements**

Ms S Banu, Librarian of L V Prasad Eye Institute, Hyderabad.

**Financial support and sponsorship**

Hyderabad Eye Research Foundation.

**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Speaker MG, Menikoff JA. Prophylaxis of endophthalmitis with topical povidone-iodine. Ophthalmology 1991;98:1769-75.
2. Pathengay A, Khera M, Das T, Sharma S, Miller D, Flynn HW Jr. Acute postoperative endophthalmitis following cataract surgery: A review. Asia Pac J Ophthalmol (Phila) 2012;1:35-42.
3. Ciulla TA, Starr MB, Masket S. Bacterial endophthalmitis prophylaxis for cataract surgery: An evidence-based update. Ophthalmology 2002;109:13-24.
4. Haripriya A, Chang DF, Ravindran RD. Endophthalmitis reduction with intracameral moxifloxacin prophylaxis: Analysis of 600 000
surgeries. Ophthalmology 2017;124:768-75.
5. 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.
6. Galvis V, Tello A, Sanchez MA, Camacho PA. Cohort study of intracameral moxifloxacin in postoperative endophthalmitis prophylaxis. Ophthalmy Eye Dis 2014;6:1-4.
7. Barry P. Intracameral antibiotic prophylaxis: American paper mirrors European experience. J Cataract Refract Surg 2013;39:2-3.
8. 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.
9. Zhou AX, Messenger WB, Sargent S, Ambati BK. Safety of undiluted intracameral moxifloxacin without postoperative topical antibiotics in cataract surgery. Int Ophthalmol 2016;36:493-8.
10. Storey P, Dollin M, Pitcher J, Reddy S, Vojtko J, Vander J, et al. The role of topical antibiotic prophylaxis to prevent endophthalmitis after intravitreal injection. Ophthalmology 2014;121:283-9.
11. Available from: https://www.asrs.org/content//2014_global_trends_comprehensivepostmg.pdf. [Last accessed on 2019 Apr 14].
12. Maharana PK, Chhablani JK, Das TP, Kumar A, Sharma N. All India Ophthalmological Society members results cataract surgery antibiotic prophylaxis current practice pattern 2017. Indian J Ophthalmol 2018;66:820-4.
13. Barry P. Adoption of intracameral antibiotic prophylaxis of endophthalmitis following cataract surgery: Update on the ESCRs Endophthalmitis Study. J Cataract Refract Surg 2014;40:138-42.
14. Barry P, Seal DV, Gettinby G, Lees F, Peterson M, Revie CW, et al. ESCRS study of prophylaxis of postoperative endophthalmitis after cataract surgery: Preliminary report of principal results from a European multicenter study. J Cataract Refract Surg 2006;32:407-10.
15. Yoshida J, Kim A, Pratzer KA, Stark WJ. Aqueous penetration of moxifloxacin 0.5% ophthalmic solution and besifloxacin 0.6% ophthalmic suspension in cataract surgery patients. J Cataract Refract Surg 2010;36:1499-502.
16. 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.
17. Results of the Endophthalmitis Vitrectomy Study. A randomized trial of immediate vitrectomy and of intravenous antibiotics for the treatment of postoperative bacterial endophthalmitis. Endophthalmitis Vitrectomy Study Group. Arch Ophthalmol 1995;113:1479-96.
18. Available from: www.npcb.nic.in. [Last accessed on 2018 May 02].
19. King DE, Malone R, Lilley SH. New classification and update on the quinolone antibiotics. Am Fam Physician 2000;61:2741-8.
20. Duggirala A, Joseph J, Sharma S, Nutheti R, Garg P, Das T. Activity of newer fluoroquinolones against gram-positive and gram-negative bacteria isolated from ocular infections: An in vitro comparison. Indian J Ophthalmol 2007;55:15-9.
21. World health organization. WHO guidelines for safe surgery 2009. World Health Organization 2009. Available from: http://www.who.int/gpsc. [Last accessed on 2016 Nov 21].