Original Article

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

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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

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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 acute 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.[15]

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).[16] Intracameral cefuroxime and moxifloxacin, with proven safety and efficacy, were used in the study.[4,13,16] 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.[16] In brief, the study included patients who underwent cataract

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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 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). Hydroxyl propyl methyl cellulose was the viscoelastic used in all eyes. All patients received intracameral antibiotic, preselected for ICC or ICM (described in EPS # 1).[16] 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), refracted 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 (EVS).[17] 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 the18-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 17,855 (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 antibiotics (1 per 2231 operated eyes that did not receive topical antibiotic). This was not statistically significant (P = 0.376) [Fig. 1]. Similarly, in the ICC 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 intracameral 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).

Table 1: Baseline differences between the two groups

	Postoperative Topical Antibiotic No	Postoperative Topical Antibiotic Yes	*P*
Total number	17 855 (42.0-%)	24 611 (58.0-%)	
Paying status of patients			
Paying	5117 (28.66%)	7454 (30.29%)	<0.001[a]
Not paying	12 738 (71.34%)	17 157 (69.71%)	
Gender			
Male	7788 (43.62%)	10562 (42.92%)	0.149
Female	10067 (56.38%)	14049 (57.08%)	
Eye			
Right eye	9473 (53.06%)	13048 (53.02%)	0.938
Left eye	8382 (46.94%)	11563 (46.98%)	
Surgery technique			
Phacoemulsification	2248 (12.59%)	3804 (15.46%)	<0.001[a]
SICS[b]	15 607 (87.41%)	20 807 (84.54%)	
Complications			
No	17 669 (98.96%)	23 625 (95.99%)	<0.001[a]
Yes	186 (1.04%)	986 (4.01%)	
Surgeon category			
Faculty	2538 (14.21%)	5446 (22.13%)	<0.001[a]
Fellow	14396 (80.63%)	17321 (70.38%)	
Resident	921 (5.16%)	1844 (7.49%)	
Intracameral antibiotics			
Cefuroxime	5723 (32.05%)	12209 (49.61%)	<0.001[a]
Moxifloxacin	12132 (67.95%)	12402 (50.39%)	
Endophthalmitis			
No	17847 (99.96%)	24604 (99.97%)	0.376
Yes	8 (0.045%)	7 (0.028%)	

[a]*P*<0.05 was statistically significant. [b]SICS – small incision cataract surgery

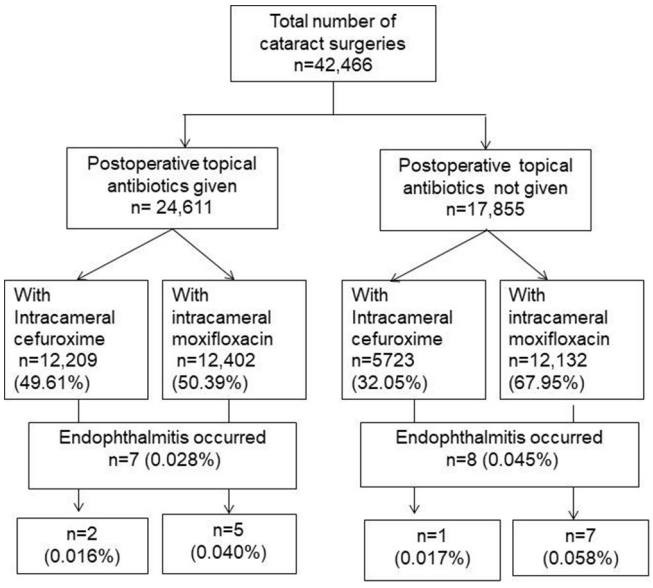

Figure 1: Endophthalmitis with and without topical antibiotics. Flow chart showing distribution of cases in different groups

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;[4,5,7,13,16] and that postoperative topical antibiotic may not be mandatory.[9] 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).[16] (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.[18] In our earlier study, we reported an annual savings of INR 6-130 million

Table 2: Incidence and association of endophthalmitis with and without specific topical postoperative after intracameral antibiotic

Intracameral antibiotic	Postoperative topical antibiotic	*n*	Endophthalmitis *n* (%)	*P*
Cefuroxime *n*=17,932	No topical antibiotic prescribed	5,723	1 (0.017)	
	Topical antibiotic prescribed			
	Ciprofloxacin	9,137	2 (0.022)	0.854
	Ofloxacin	707	0	
	Moxifloxacin	2,365	0	
Moxifloxacin *n*=24,534	No topical antibiotic prescribed	12,132	7 (0.058)	
	Topical antibiotic prescribed			
	Ciprofloxacin	8,954	4 (0.045)	0.682
	Ofloxacin	2,591	1 (0.039)	0.705
	Moxifloxacin	857	0	

Table 3: Occurrence of endophthalmitis with phacoemulsification and SICS with or without antibiotic in postoperative period

Surgical technique	Postoperative topical antibiotic	No endophthalmitis occurred	Occurrence of endophthalmitis	Total	*P*
Phacoemulsification (*n*=6052)	No	2247	1 (0.044%)	2248	
	Yes	3803	1 (0.026%)	3804	0.707
SICS[a] (*n*=36,414)	No	15600	7 (0.045%)	15607	
	Yes	20801	6 (0.028%)	20807	0.423

[a]SICS – Small incision cataract surgery

Table 4: Annual cost savings of eliminating topical fluoroquinolone in cataract surgery

Total cataract surgery in year 2016-17 in India: 6.481 million				
Treatment schedule				
Intracameral antibiotic	Endophthalmitis rate	0.035%	Endophthalmitis Possibilities	2268 eyes
Topical antibiotics		0.028%		1815 eyes
No topical antibiotic		0.045%		2916 eyes
No Ciprofloxacin	Unit cost	Rs 17.00	Savings	INR110 million (USD 1.6 million)
No Moxifloxacin		Rs 117.00		INR 758 million (USD 11.6 million)

because of managing reduced number of endophthalmitis after intracameral antibiotic.[16] 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).[19] 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.[20]

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.[21]

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Conflicts of interest

There are no conflicts of interest.

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