

# Endophthalmitis reduction with intracameral moxifloxacin in eyes with and without surgical complications: Results from 2 million consecutive cataract surgeries



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**Purpose:** To analyze the posterior capsule rupture (PCR) rates among staff and trainee cataract surgeons, and the postoperative endophthalmitis (POE) rates in uncomplicated and complicated eyes both with and without intracameral moxifloxacin prophylaxis (ICMP).

**Setting:** Ten regional Aravind Eye Hospitals in India.

**Design:** Retrospective multicenter clinical registry within a single hospital network.

**Methods:** POE rates with and without ICMP were statistically compared for all eyes and separately for trainees versus staff, for phacoemulsification versus manual small-incision cataract surgery (M-SICS), and for a subgroup of eyes complicated by PCR or requiring secondary surgery.

**Results:** All cataract surgeries (2 062 643) performed during the 8-year period from 2011 to 2018 at the 10 regional Aravind Eye hospitals were included in the analysis. With ICMP, the overall

POE rate declined from 692 (0.07%) of 993 009 eyes to 185 (0.02%) of 1 069 634 eyes ( $P < .001$ ). This was independently significant for phacoemulsification and for M-SICS ( $P < .001$ ). The overall PCR rate was 28 352 (1.37%) of 2 062 643 eyes, and it was statistically higher for trainees irrespective of surgical method ( $P < .001$ ). Both staff and trainee surgeons had higher PCR rates with phacoemulsification than with M-SICS ( $P < .001$ ). Absent ICMP, PCR increased the overall POE rate by more than 7-fold to 63 (0.43%) of 14 505 eyes. ICMP reduced the POE rate after PCR to 25 (0.18%) of 13 847 eyes ( $P = .002$ ). This ICMP benefit was separately significant for both M-SICS (0.54% vs 0.26%,  $P = .01$ ) and phacoemulsification (0.29% vs 0.06%,  $P = .005$ ). The POE rate was especially high after secondary IOL implantation (0.90% without ICMP vs 0.34% with ICMP;  $P = .10$ ).

**Conclusions:** ICMP reduced the POE rate overall, with phacoemulsification, with M-SICS, and in eyes with PCR.

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It is widely acknowledged that posterior capsule rupture (PCR) is a risk factor for postoperative endophthalmitis (POE). A 2013 meta-analysis of 42 studies<sup>1</sup> found that PCR increased the pooled risk for POE by more than 6-fold. In a 2015 study using the United Kingdom's Royal College of Ophthalmologists' National Ophthalmology Database,<sup>2</sup> PCR increased the POE rate by 8-fold during a 4-year period encompassing more than 180 000 consecutive surgeries. A 2016 study of more than 315 000 cases during a 7-year period at Kaiser Permanente<sup>3</sup> found that PCR was associated with a 3.68-fold increase in POE. Finally, a 2016 study using the French National Database<sup>4</sup> estimated a 5-fold increase in post-cataract POE associated with perioperative vitrectomy during a 5-year period.

To our knowledge, the use of antibiotic prophylaxis to prevent POE in eyes that have experienced PCR has not been specifically studied. Mounting evidence suggests that intracameral (IC) antibiotic prophylaxis reduces the rate of POE with cataract surgery.<sup>1–16</sup> However, wider international adoption of routine IC antibiotic prophylaxis continues to be limited by a lack of approved commercial formulations and limited prospective, randomized controlled data.<sup>11,17</sup> We previously published data on the efficacy of routine intracameral moxifloxacin prophylaxis (ICMP) during a 29-month period at the Aravind Eye Care System (AECS), a network of 12 regional eye hospitals in southern India, which performs more than 260 000 cataract surgeries annually.<sup>9</sup> The current study was undertaken to analyze the PCR rates, the POE rates, and the rate

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of POE after PCR at the AECS over an 8-year period, and to compare these POE rates with and without ICMP.

## PATIENTS AND METHODS

### Study Design

This retrospective clinical registry-based study evaluated all charity and private patients who had cataract surgery between January 1, 2011 and December 31, 2018 at the 10 established regional AECS hospitals. Data from two centers (Coimbatore city center and Chennai), which did not open until November 2014 and September 2017, respectively, were not included in the analysis. The study was approved by the AECS institutional review board and ethics committee. All study procedures adhered to the principles outlined in the Declaration of Helsinki.

Charity patients either presented to a regional hospital or were transported from outreach camps to a regional hospital where they had surgery for little to no fee. The majority of these patients had manual small-incision cataract surgery (M-SICS) with a poly(methyl methacrylate) intraocular lens (IOL). Private patients paid market rates to primarily have phacoemulsification with a foldable IOL at the same regional hospitals. M-SICS with a poly(methyl methacrylate) IOL was performed in a few private patients because of severe cataract density. Large-incision manual extracapsular cataract surgery (ECCE) was performed by staff in select patients who were at a higher risk for complications or by trainees as a prerequisite to learning M-SICS.

Perioperative medication regimens for cataract surgery are standardized at all AECS hospitals. All patients received topical ofloxacin prophylaxis preoperatively and postoperatively throughout the study period. No IC antibiotic prophylaxis was used prior to August 14, 2014, when routine IC injection of 0.1 mL of moxifloxacin 0.5% weight per volume (Auromox) at the conclusion of surgery was instituted for all charity patients at the Madurai hospital. Based on the efficacy of ICMP on the POE rate in this population, which was subsequently reported,<sup>18</sup> all 10 AECS hospitals adopted routine ICMP for all cataract surgeries. The transition to routine ICMP at each hospital was made between April 9, 2015 and July 1, 2015. The period from January 2011 to December 2018 was chosen for this study because it included roughly equal numbers of consecutive cataract surgeries performed with and without ICMP.

Auromox is commercially approved and available in India. As previously reported, 1 mL of the solution containing 5 mg of preservative-free moxifloxacin hydrochloride is packaged in sterile glass vials so that no mixing or dilution is required for intraocular injection. All eyes receiving ICMP had an injection of 0.1 mL containing 0.5 mg of moxifloxacin into the anterior segment at the conclusion of surgery.

Preoperatively, all cataract patients received a standardized regimen of topical ofloxacin eyedrops (0.5 mg/5 mL, Auroflox) every 3 hours on the day before surgery and twice on the morning of surgery. Topical povidone-iodine was used immediately before surgery to prepare the periorbital area (10%) and the conjunctival cul-de-sac (5%). Topical ofloxacin drops were instilled 4 times a day for the first 15 days postoperatively. In addition, a topical combination solution of gatifloxacin (3 mg/10 mL) and dexamethasone (1 mg/10 mL) (Gatilox DM) was administered 8 times per day for the first postoperative week, and then tapered off over the next 4 to 6 weeks. Despite the redundancy with the ofloxacin, this combination topical drop is routinely used at AECS because it is the lowest cost topical steroid formulation available to the regional patient population. All patients were examined on the first postoperative day and at approximately 1 month postoperatively by an ophthalmologist, who diagnosed and treated any postoperative complications.

The AECS electronic health record (EHR) system was developed internally for documenting surgical outcomes, and it has been used at all AECS hospitals and clinics since 2008.

Preoperative, operative, and postoperative data for every AECS patient undergoing cataract surgery is entered by scribes. Additional study data were drawn from the medical records database and from microbiology department records. The EHRs of any study patients with a coded diagnosis of endophthalmitis, PCR, or secondary surgical intervention occurring during the 6-week postoperative period were reviewed and analyzed. All secondary IOL procedures performed within 3 months of the primary surgery were analyzed separately.

During the 6-week postoperative period, any patient suspected of having POE by the examining physician was reevaluated by a senior medical officer to confirm the diagnosis. A vitreous tap was performed for culture and simultaneous antibiotic injection in any eye diagnosed with POE. A vitrectomy was performed in addition to or instead of a vitreous tap in some cases.

To assess the effect of IC antibiotic prophylaxis, the POE rates between the two cataract patient populations that did and did not receive ICMP were compared, including separate subanalyses for phacoemulsification, M-SICS, or manual ECCE. All cases with PCR (with and without vitreous loss) both in aggregate, and separately for each type of procedure, were tabulated to determine which surgical method had the lowest PCR rate. To assess the effect of surgical inexperience, the PCR rates for each procedure were compared separately for both staff and trainee surgeons. The latter category included residents, fellows, and visiting trainees who were practicing ophthalmologists from other centers or countries that enrolled in surgical skill transfer programs at AECS. Trainees typically performed 10 to 15 ECCE procedures before learning M-SICS, and at least 100 M-SICS procedures before learning phacoemulsification. Finally, the POE rates in patients who did and did not experience PCR were compared, as well as the effect of ICMP on the POE rates in eyes complicated by PCR or that had reoperations.

### Statistical Analysis

All analyses were carried out using SPSS Statistics software (version 17.0, SPSS, Inc.) or STATA software (version 11.1, StataCorp LP). Categorical variables were expressed as a frequency (percentage). A *P* value less than 0.05 was considered statistically significant.

## RESULTS

Between 2011 and 2018 (8 years), 2 062 643 consecutive cataract surgeries were performed at the 10 AECS hospitals. Of those, 993 009 eyes did not receive ICMP and 1 069 634 eyes did receive ICMP. After initiating routine ICMP, the overall AECS POE rate declined significantly from 692 (0.07%) of 993 009 eyes to 185 (0.02%) of 1 069 634 eyes (*P* < .001) (Table 1). The POE rate reduction with ICMP was also statistically significant for both M-SICS and phacoemulsification when separately analyzed (*P* < .001) (Table 1). Figure 1 shows a comparison between sequential quarterly POE rates during the study period, along with the quarterly surgical volumes. The complete transition to routine ICMP throughout the entire AECS occurred over a 1-year period. This is because ICMP was initially started for M-SICS patients at the Madurai hospital before being adopted on varying initiation dates at all AECS centers.<sup>18</sup> This data analysis shows a consistent reduction in POE rates associated with ICMP across the study period.

PCR was noted in 28 352 (1.37%) eyes, of which 24 913 eyes (87.9%) had concomitant vitreous loss and the remaining 3 432 eyes (12.1%) did not. Table 2 shows that the PCR rate was statistically higher for trainees compared

**Table 1. Comparison of endophthalmitis rates without ICMP and with ICMP, according to surgical method for 2 062 643 consecutive cataract surgeries.**

Technique	Without ICMP		With ICMP		P Value*
	Surgeries, n	Endophthalmitis, n (%)	Surgeries, n	Endophthalmitis, n (%)	
ECCE	23 003	22 (0.10)	9363	3 (0.03)	.06
M-SICS	676 774	495 (0.07)	725 234	144 (0.02)	< .0001
Phaco	293 232	175 (0.06)	335 037	38 (0.01)	< .0001
Total	993 009	692 (0.07)	1 069 634	185 (0.02)	< .0001

ECCE = extracapsular cataract extraction; ICMP = intracameral moxifloxacin prophylaxis; M-SICS = manual small-incision cataract surgery; Phaco = phacoemulsification  
 \*P value between the group with ICMP and the group without ICMP group (Fisher exact test)

with staff surgeons both overall, and for each of the three different surgical methods. Both staff and trainee surgeons had higher PCR rates with phacoemulsification than with M-SICS; however, the difference was especially pronounced in the trainee group ( $P < .001$ ).

Tables 3A and 3B show the effect of PCR on the POE rate in patients who did not receive ICMP and those who did receive ICMP, respectively. PCR statistically increased the rate of POE both overall and for every surgical method. In the absence of ICMP, PCR was associated with nearly a 5-fold increase in the phacoemulsification POE rate, a nearly 8-fold increase in the M-SICS POE rate, and more than a 7-fold increase in the overall POE rate (Table 3A). In patients receiving ICMP, PCR was associated with a 6.0-fold increase in the phacoemulsification POE rate, a 13-fold increase in the M-SICS POE rate, and a 12-fold increase in the overall POE rate (Table 3B).

An analysis of eyes with PCR showed that 63 (0.43%) of the 14 505 eyes that did not receive ICMP and 25 (0.18%) of 13 847 eyes that did receive ICMP developed POE ( $P = .002$ ) (Table 4). The 2.3-fold overall reduction in

the POE rate after PCR that was associated with ICMP was also separately significant for both M-SICS ( $P = .01$ ) and phacoemulsification ( $P = .005$ ). Table 4 also shows PCR cases analyzed separately for staff and trainee surgeons. For staff cases, ICMP was associated with a much lower POE rate after PCR than without ICMP ( $P = .0007$ ). However, this difference was not significant for trainee surgeons.

Secondary surgical procedures during the immediate 6-week postoperative period were performed in 14 065 eyes (0.68%) as shown in Table 5. The secondary surgeries included anterior chamber washout, wound repair, IOL repositioning, secondary IOL implantation, and anterior or pars plana vitrectomy. Secondary IOL implantations were performed for aphakia or IOL exchange and included anterior chamber IOLs and sulcus-, iris-, or scleral-fixated posterior chamber IOLs. Among these reoperated eyes, approximately equal numbers did and did not receive ICMP (6952 vs 7113). In eyes undergoing secondary surgical intervention, ICMP was associated with a reduction in the POE rate from 0.12% to 0.06%, but this

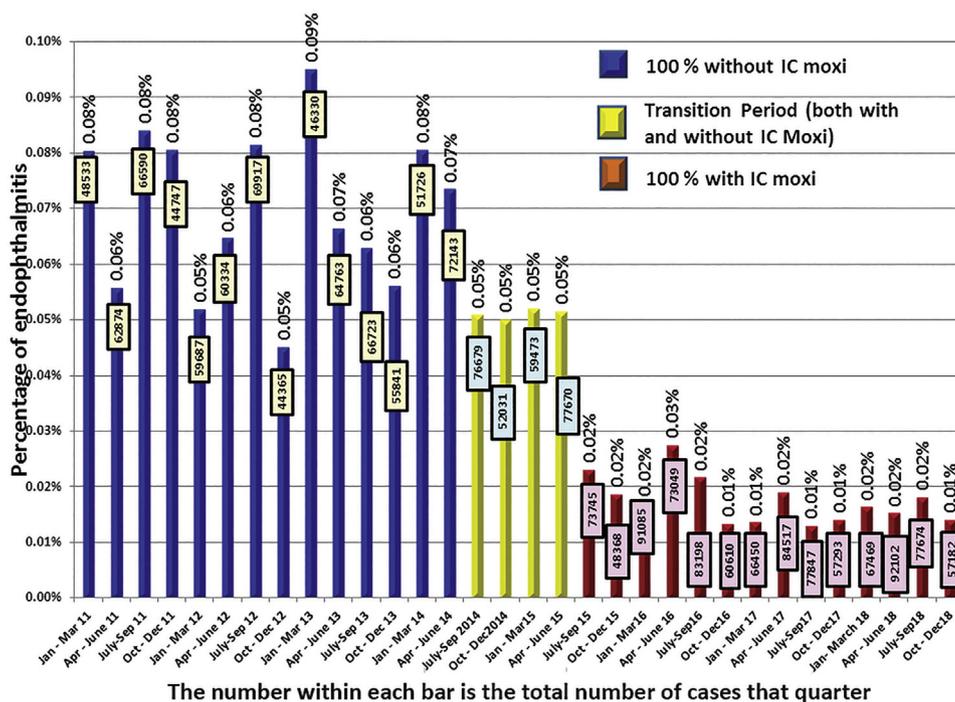


Figure 1. Quarterly rates of post-operative endophthalmitis at Aravind hospitals from January 2011 to December 2018 (IC moxi = intracameral moxifloxacin).

**Table 2. Comparison of PCR rate between different surgeon groups for each of the 3 surgical techniques.**

Surgeon Category/TSV	PCR Rate											
	Phaco			M-SICS			ECCE			All 3 Techniques		
	N (%)	OR (95% CI)	P Value*	N (%)	OR (95% CI)	P Value*	N (%)	OR (95% CI)	P Value*	N (%)	OR (95% CI)	P Value*
Staff 1 401 088	7211 (1.24)	1	<.001	8610 (1.06)	1	<.001	317 (3.62)	1	<.001	16 138 (1.15)	1	<.001
Trainee 661 555	2593 (5.40)	4.53 (4.33, 4.75)	—	8505 (1.44)	1.37 (1.32, 1.41)	—	1116 (4.73)	1.32 (1.16, 1.5)	—	12 214 (1.85)	1.61 (1.58, 1.65)	—
Overall 2 062 643	9804 (1.56)	—	—	17 115 (1.22)	—	—	1433 (4.43)	—	—	28 352 (1.37)	—	—

ECCE = extracapsular cataract extraction; CI = confidence interval; M-SICS = manual small-incision cataract surgery; OR = odds ratio; PCR = posterior capsule rupture; Staff = medical officers; Trainee = residents, fellows, and visiting trainees; TSV = total surgical volume

\*Staff vs trainee. To compare staff vs trainee complication rates, the staff rate was used as the reference value for the OR and P value calculations (Number of P < .001 for phacoemulsification vs the M-SICS complication rate comparison). The P values between the two groups were determined with logistic regression

difference was not statistically significant (P = .23). The POE rate was particularly high in eyes undergoing secondary IOL implantation, reaching 0.9% in eyes without ICMP and 0.34% in eyes with ICMP (P = .14).

Table 6 shows the culture results for all POE cases, which were tabulated according to whether ICMP was administered. The majority of eyes in both groups were culture-negative (62% vs 48%; P = .23). There was a statistically significant decrease in POE due to of coagulase-negative *Staphylococcus* with ICMP (90 [0.009%] of 993 009 eyes vs 12 [0.001%] of 1 069 634 eyes; P = .013). ICMP was not associated with any adverse events. Specifically, no instances of toxic anterior segment syndrome or corneal decompensation were attributed to the antibiotic injection. The overall rate of persistent postoperative corneal edema (1 month or longer) was not higher in the ICMP group compared with the no ICMP group.

**DISCUSSION**

To our knowledge, our consecutive series of 28 352 cases of PCR is one of the largest ever reported (Table 2). The overall PCR rate of 1.37% from more than 2 000 000 consecutive cataract surgeries compares favorably with other large

retrospective trials.<sup>19–21</sup> This series expands on an earlier study from the Madurai Aravind Regional Hospital,<sup>22</sup> demonstrating a significantly higher PCR rate among our trainees compared with staff surgeons (Table 2). Although the PCR rate was statistically higher with phacoemulsification than with M-SICS for both surgeon groups, the difference was especially notable for trainees who had more than a 4-fold higher PCR rate with phacoemulsification. This multicenter AECS data confirms our earlier single hospital finding that the learning curve is much more complication-prone with phacoemulsification than with M-SICS for inexperienced surgeons.<sup>22</sup>

In the absence of ICMP, PCR increased the overall POE rate by more than 6-fold, demonstrating how much higher the risk for POE rises after this complication (Table 3A). This is in line with the relative risk reported from other large databases, which unlike ours, were not derived from a single hospital network.<sup>2–4</sup> The posterior capsule forms a natural anatomic barrier between the anterior and posterior segments. A defect in this barrier, especially if accompanied by disruption of the hyaloid face, provides access to the vitreous cavity for any microbes contaminating the anterior segment. In addition, an anterior

**Table 3A. Comparison of POE rates between eyes with PCR and eyes with no PCR without ICMP.**

Technique	Without ICMP				
	Surgeries, n	Eyes w/PCR, n (%)	POE in Eyes w/PCR, n (%)	POE in Eyes w/o PCR, n (%)	P Value*
ECCE	23 003	1120 (4.87)	3 (0.27)	19 (0.09)	.0645
M-SICS	676 774	8576 (1.27)	46 (0.54)	449 (0.07)	<.0001
Phaco	293 232	4809 (1.64)	14 (0.29)	161 (0.06)	<.0001
Total	993 009	14 505 (1.46)	63 (0.43)	629 (0.06)	<.0001

ECCE = extracapsular cataract extraction; ICMP = intracameral moxifloxacin prophylaxis; M-SICS = manual small-incision cataract surgery; PCR = posterior capsule rupture; Phaco = phacoemulsification; POE = postoperative endophthalmitis

\*P value between two groups (proportion test)

Technique	With ICMP				
	Surgeries, n	Eyes w/PCR, n (%)	POE in Eyes w/PCR, n (%)	POE in Eyes w/o PCR, n (%)	P Value*
ECCE	9363	313 (3.34)	0 (0.00)	3 (0.03)	.75
M-SICS	725 234	8542 (1.18)	22 (0.26)	122 (0.02)	<.0001
Phaco	335 037	4992 (1.49)	3 (0.06)	35 (0.01)	.0007
Total	1 069 634	13 847 (1.29)	25 (0.18)	160 (0.015)	<.0001

ECCE = extracapsular cataract extraction; ICMP = intracameral moxifloxacin prophylaxis; M-SICS = manual small-incision cataract surgery; PCR = posterior capsule rupture; Phaco = phacoemulsification; POE = postoperative endophthalmitis

\*P value between two groups (proportion test)

vitrectomy further disturbs the vitreous, introduces infusion into the posterior segment, and creates a much larger unicameral chamber from which microbial contamination might be more difficult to eradicate. This much larger volume of distribution would also significantly lower the antibiotic concentration achieved with a 0.1 mL intraocular injection. That ICMP did not prevent the POE rate from rising after PCR in our study raises the question of whether a larger IC volume of 0.5% moxifloxacin should be instilled after anterior vitrectomy.

In this large consecutive series of 28 352 patients with PCR, ICMP significantly reduced the POE rate both overall as well as for phacoemulsification and M-SICS individually (Table 4). Most relevant to Western ophthalmologists is that phacoemulsification patients with PCR had a 4.8-fold reduction in the POE rate in the ICMP group to only 3 (0.06%) of 4992 eyes, which compares favorably to global POE rates reported without PCR or IC antibiotic stratification.<sup>23</sup> It is important to note that even with ICMP, the overall POE rate was significantly higher after PCR (0.18%), as well as in the phacoemulsification and M-SICS subgroups. In approximately 6000 patients with perioperative vitrectomy coded in the operative report, the French national study found a reduction in POE from 0.51% to 0.37% associated with IC cefuroxime ( $P = .001$ ). This study methodology was unable to identify cases of PCR without anterior vitrectomy, however.

The current study allows us to expand our previously reported retrospective analysis of ICMP efficacy in 617 453 eyes.<sup>9</sup> In this much larger series of 2 062 643 consecutive eyes, we found that ICMP was associated with a 3.5-fold POE rate reduction both overall and for M-SICS, and a 6-fold POE rate reduction for phacoemulsification. That these results replicate those of our previous study<sup>9</sup> further strengthens the evidence that ICMP is effective in reducing POE. As in our previous analysis, there was a significant reduction in coagulase-negative *Staphylococcus* POE with ICMP, despite the higher reported rates of quinolone resistance among such endophthalmitis isolates.<sup>9,23</sup> We believe this apparent efficacy is attributable to the high IC moxifloxacin concentration achieved by direct injection, and the fact that the characterization of antibiotic resistance is based on serum concentrations measured after systemic administration.<sup>24</sup>

Because PCR inflates the POE risk so much, it is useful to separately assess the effect of ICMP both in eyes with PCR and in a surgical population that excludes PCR (Tables 3A and 3B). That ICMP statistically lowered POE in both groups suggests benefit for both high-risk and low-risk cataract patients (Table 4). Since instituting routine ICMP, POE occurred in only 35 of 335 037 consecutive eyes undergoing phacoemulsification without concomitant PCR. This extremely low 0.01% POE rate is especially

**Table 4. Comparison of POE rates in eyes with PCR without ICMP and with ICMP, including a subanalysis of different procedures and different surgeon groups.**

Procedure or Surgeon Group	Without ICMP		With ICMP		P Value*
	Eyes w/PCR, n	POE in Eyes w/PCR, n (%)	Eyes w/PCR, n	POE in Eyes w/PCR, n (%)	
ECCE <sup>†</sup>	1120	3 (0.27)	313	0 (0.00)	.42
M-SICS <sup>†</sup>	8576	46 (0.54)	8542	22 (0.26)	.01
Phaco <sup>†</sup>	4809	14 (0.29)	4992	3 (0.06)	.005
Staff	7874	41 (0.52)	8029	16 (0.19)	.0007
Trainee	6631	22 (0.33)	5818	9 (0.15)	.26
Total	14 505	63 (0.43)	13 847	25 (0.18)	.002

ECCE = extracapsular cataract extraction; ICMP = intracameral moxifloxacin prophylaxis; M-SICS = manual small-incision cataract surgery; PCR = posterior capsule rupture; Phaco = phacoemulsification; POE = postoperative endophthalmitis; Staff = medical officers; Trainee = residents, fellows, and visiting trainees

\*P value between two groups (proportion test)

<sup>†</sup>All surgeons

**Table 5. Endophthalmitis rate in each type of reoperation without ICMP and with ICMP.**

Reoperation Type	Without ICMP		With ICMP		Total Reoperation, n (% of All Surgeries)	Total POE, n (%)
	Reoperation, n (% of All Surgeries)	POE n, (%)*	Reoperation, n (% of All Surgeries)	POE n, (%)*		
Anterior chamber washout	2399 (0.24)	1 (0.04)	2835 (0.27)		5234 (0.25)	1 (0.02)
Wound suturing/iris abscission	1245 (0.13)		1096 (0.10)	1 (0.09)	2341 (0.11)	1 (0.04)
IOL reposition	1103 (0.11)		1162 (0.11)		2265 (0.11)	
Secondary IOL <sup>†</sup>	779 (0.08)	7 (0.90)	875 (0.08)	3 (0.34)	1654 (0.08)	10 (0.60)
PPV for dislocated nucleus/epinucleus/IOL	573 (0.06)		279 (0.03)		852 (0.04)	
Anterior vitrectomy	329 (0.03)		311 (0.03)		640 (0.03)	
Other	524 (0.05)		555 (0.05)		1079 (0.05)	
Total	6952 (0.70)	8 (0.12)	7113 (0.66)	4 (0.06)	14 065 (0.68)	12 (0.09)

ICMP = intracameral moxifloxacin prophylaxis; IOL = Intraocular lens; POE = postoperative endophthalmitis; PPV = pars plana vitrectomy

\*None of the differences in endophthalmitis rates between the groups with ICMP and without ICMP reached statistical significance

<sup>†</sup>Secondary IOLs included scleral-fixated, sulcus-fixated, and iris-fixated posterior chamber IOLs and anterior chamber IOLs

noteworthy considering AECS’s routine reuse of gowns, gloves, surgical tubing, irrigating solutions, and a number of instruments and drugs limited to single use in the United States. These and other practices, such as having multiple patients share the same operating room, would not be permitted in many countries because of infection concerns.<sup>25</sup> Despite significant differences in operating room practices, our overall 0.01% phacoemulsification POE rate with ICMP compares favorably with the 0.04% to 0.05% POE rates from the American Academy of Ophthalmology IRIS registry,<sup>A</sup> which includes cases both with and without IC antibiotic prophylaxis.<sup>26</sup> The low POE rates reported with ICMP in this trial raises the thought-provoking possibility that many expensive and environmentally wasteful infection control practices in Western operating rooms might be unnecessary and deserving of further study.<sup>27</sup>

The large size of this study population provides important new data on POE rates associated with different types of secondary surgical intervention during the first 6

postoperative weeks (Table 5). The POE rate was very high for secondary IOL implantation performed for aphakia or IOL exchange. Many of these eyes lacked an intact posterior capsule, and the absence of this anatomic barrier might explain the higher POE rate.

For secondary IOL implantation, ICMP was associated with a greater than 2.5-fold reduction in POE, but this did not reach statistical significance for this population size (n = 1654). POE was uncommon with other secondary surgical procedures. Although rare after phacoemulsification, postoperative hyphema is more commonly encountered with M-SICS, which explains the relatively high number of anterior chamber washout procedures.

All AECS facilities employ an identical EHR system. Uniform EHR reporting protocols provide a large real-time registry through which we continuously monitor clinical outcomes and specific complications such as PCR, POE, and early postoperative secondary surgical intervention. However, compared with other

**Table 6. Culture results for endophthalmitis cases in eyes without ICMP and with ICMP.**

Culture Type	Without ICMP (n = 993 009)	%	With ICMP (n = 1 069 634)	%	P Value*
Negative culture	489	0.05	147	0.01	<.0001
Coagulase-negative <i>Staphylococcus</i>	90	0.009	12	0.001	<.0001
<i>Staphylococcus aureus</i>	9	0.0009	5	0.0004	.15
<i>Streptococcus species</i>	24	0.002	4	0.0003	.0003
<i>Nocardia species</i>	37	0.004	8	0.0007	.0001
Other gram-positive species	7	0.0007	2	0.0002	.03
<i>Pseudomonas aeruginosa</i>	9	0.0009	0	0	.001
Other gram-negative bacteria	15	0.0015	3	0.0002	.017
Fungus	8	0.0008	3	0.0002	.05
Atypical mycobacterium	3	0.0003	1	0.0001	.2
Total number of endophthalmitis cases	692	0.07	185	0.02	<.0001

ICMP = intracameral moxifloxacin prophylaxis

\*Two-sample proportion test

large registries, such as from a national database, the AECS patient population is unique for its level of standardization of both perioperative and surgical care. Because approximately 60% of our cataract surgeries are performed in charity patients, the AECS follows standardized preoperative, surgical, and postoperative protocols throughout its regional hospital network to maximize efficiency, cost-effectiveness, and economies of scale. This includes using the same perioperative topical antibiotic and antiinflammatory medications and dosing; the same manufacturers and brands for ophthalmic viscosurgical devices, irrigating solutions, IOLs, and blades; and uniform protocols for anesthesia, prepping, draping, and instrument cleaning and sterilization. Such standardization reduces potential confounding variables, and it is generally lacking from other published multicenter studies.

Nonrandomized retrospective trials introduce the potential for other variables to influence the results. Although 8-year retrospective trials such as ours generate larger study populations, they also increase the chance that differences in surgical techniques or in surgeon and patient populations could have separately reduced the infection rate. Although we acknowledge these drawbacks to any retrospective study, we believe that the exceptionally high volume of patients compared over a relatively short period of time within a single hospital network with universal standardized protocols makes our data on ICMP efficacy more convincing. The reduction in POE with ICMP was statistically significant regardless of whether a 1-, 2-, 4-, 6-, or 8-year consecutive period is analyzed. The second quarter of 2016 had the highest POE rate with ICMP (0.03%). However, this was statistically lower than the POE rates from all but one of the 14 quarters without ICMP. Furthermore, selecting and comparing any 2 quarters with and without ICMP (Figure 1) would provide a study size of more than 100 000 eyes. The ESCRS prospective, randomized trial only reported results from approximately 16 000 eyes.<sup>6</sup> Finally, it would be impossible to randomize more than 28 000 consecutive cases of PCR, considering that over 2 000 000 procedures were required to generate this number of complications.

Clinical surveys have shown that many surgeons do not routinely employ IC antibiotic prophylaxis.<sup>17</sup> Reasons cited include cost, lack of commercially approved antibiotic formulations, the risk for toxic anterior segment syndrome from compounded drugs, concern about fostering antibiotic resistance, and unproven need based on the paucity of level 1 evidence.<sup>11,17,28,29</sup> However, because PCR so significantly increases the POE rate, and based on the results from this large retrospective series, we recommend that IC antibiotic prophylaxis be strongly considered for eyes complicated by PCR or undergoing secondary IOL implantation after previous PCR.

### WHAT WAS KNOWN

- Numerous retrospective studies show that intracameral (IC) cefuroxime prophylaxis is effective in reducing postoperative endophthalmitis (POE).
- The POE incidence is higher in eyes with surgical complications such as posterior capsule rupture (PCR).

### WHAT THIS PAPER ADDS

- In a study of more than 28 000 consecutive eyes with PCR, the POE rate was more than 7 times higher compared with uncomplicated cases.
- In one of the largest series to date (> 2 000 000 eyes), IC moxifloxacin prophylaxis significantly reduced POE in both phacoemulsification and manual small-incision cataract surgery, and in eyes with surgical complications such as PCR.

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