Asian J Ophthalmol. 2021;19:19-39
© Asian Journal of Ophthalmology

Review Article
https://doi.org/10.35119/asjoo.v18i1.941

Incidence of post-cataract surgery endophthalmitis: a chronological review and intercontinental comparison

Qingyun Wen[1,2], **Rachel Xuan**[1,2], **Keith Ong**[1,2]
[1]Northern Clinical School , University of Sydney, Sydney, Australia; [2]Department of Ophthalmology, Royal North Shore Hospital, Sydney, Australia

Abstract

Purpose: *This review aimed to investigate the global incidence of postoperative endophthalmitis (POE) after cataract surgery over the last three decades, with a particular focus on the use of prophylactic intracameral antibiotics.*

Study design: *Literature review.*

Methods: *A literature search was performed in PubMed and Scopus. Data was collected from included studies and analyzed in IBM SPSS v27.*

Results: *A total of 63 studies from 20 regions were included. The use of prophylactic intracameral antibiotics significantly reduced POE incidence. The baseline POE incidence in studies that involved intracameral prophylaxis tended to be high. A downward linear trend in POE incidence was observed in studies that did not involve intracameral antibiotic prophylaxis. Interestingly, a study in Japan reported the use of intracameral antibiotic prophylaxis in only 10.4% of cataract surgeries with an overall POE incidence of 0.025%, which is comparable to countries that use intracameral prophylaxis routinely. Within studies from Australia, China, Europe, India, Singapore and United States, Australia had the highest POE incidence with and without intracameral prophylaxis, while China had the lowest POE incidences.*

Conclusion: *Intracameral antibiotics are an effective prophylaxis against POE. However, the incidence of POE is decreasing worldwide even without intracameral prophylaxis. The benefits of intracameral antibiotics should be weighed against its risks prior to its implementation as routine prophylaxis protocol for cataract surgery.*

Keywords: *cataract surgery, endophthalmitis, endophthalmitis prophylaxis, intracameral antibiotics*

Introduction

A rare, but serious complication of cataract surgery is endophthalmitis. Postoperative endophthalmitis (POE) after cataract surgery has been reported to affect up to 0.5% of patients[1] and can be extremely debilitating to the affected

Correspondence: Dr. Keith Ong, MBBS, FRACO, FRACS, MMed, PGCert HE, 2 Railway Avenue, Eastwood, New South Wales 2122, Australia.
E-mail: keithong@optus.net.com.au

individuals. Symptoms include ocular pain, red eye, and decreased vision.[2] Treatment regimens are invasive and include specimen collection via vitreous tap/biopsy or vitrectomy and intraocular antibiotic administration. Visual prognosis remains poor despite treatment, with only 40–57% of patients achieving a visual acuity equivalent to ≥ 6/12.[3]

A 2005 review looking at the incidence of POE worldwide reported an increase from 1992–2003 despite advances in cataract surgery techniques.[4] It was postulated that the increased incidence could be attributed to the new technique of phacoemulsification and the transition from scleral tunnels to clear corneal incisions. There is therefore a clear interest in minimizing POE complication rates, with an increasing focus on the role of prophylactic antibiotics. To our knowledge, this is the most recent meta-analysis to assess trends in POE incidence across multiple countries.

In 2007, the European Society of Cataract and Refractive Surgeons (ESCRS) published the Endophthalmitis Study, showing a five-fold decrease in POE when intracameral (IC) cefuroxime was used prophylactically at the end of the surgery.[5] Prior to this study, prophylactic regimens for cataract surgeries typically involved ensuring a sterile surgical environment with the use of povidone-iodine ± topical/subconjunctival antibiotics. The use of IC antibiotics as part of routine prophylaxis has since been recommended in the ESCRS guidelines,[1] and several systematic reviews have established a significantly reduced risk of POE with IC antibiotics.[6–8]

However, the administration of IC antibiotics has been associated with increased risks of toxic anterior segment syndrome, retinal pathology, and endothelial toxicity.[9,10] Despite the ESCRS recommendations, there is still no single approach to POE prophylaxis worldwide. While Swedish and French ophthalmologists routinely use intracameral antibiotics,[11] only 50% of US ophthalmologists and 30% of Canadian ophthalmologists use these as prophylaxis. In Japan, topical antibiotics are preferred, with only 7% of ophthalmologists adopting the use of IC antibiotics.[12]

Although the benefits of IC antibiotics are evident, the associated risks are severe, and the benefit-risk ratio should be carefully considered for each patient. To facilitate this consideration, it is imperative to understand the natural historical aspect of POE incidence: has the incidence of POE continued to increase or has it decreased? This review therefore aims to investigate the trends in POE incidence worldwide over the past three decades. We hypothesize that with improving surgical and aseptic techniques, POE incidence has decreased even outside the context of prophylactic IC antibiotics.

Methods

Literature search

A literature search was carried out in PubMed and Scopus using a predefined search strategy (Table 1). Relevant papers identified through references were also included in the review. Abstracts were screened according to the inclusion and exclusion criteria, following which full-text articles were obtained to further assess eligibility. Studies were included if they were English articles published between 2000 and 2021, if they were a randomized controlled trial or a retrospective/prospective cohort study (this included clinical registries, chart reviews, etc.), if the subjects were humans, and if they reported POE incidence as one of their primary outcomes. Studies were excluded if they included less than 1,000 eyes, if they focused on subset populations (*e.g.*, patients with pre-existing risk factors for POE or pediatric populations), if the study focused on modified cataract surgeries

Table 1. Search terms and filters used in PubMed and Scopus

Search strategy	
Database	**Keywords and MeSH terms**
PubMed	((endophthalmitis*[tiab] OR Endophthalmitis [MeSH]) AND (cataract extraction* OR Cataract Extraction [MeSH]cataract extraction* OR Cataract Extraction [MeSH] OR Lens Implantation, Intraocular [MeSH])) AND (("2000/01/01"[Date - Publication]: "3000"[Date - Publication]))
	Filters applied: Abstract, Full text, Clinical Study, Clinical Trial, Comparative Study, Controlled Clinical Trial, Evaluation Study, Government Publication, Multicenter Study, Observational Study, Pragmatic Clinical Trial, Randomized Controlled Trial, Validation Study, Humans, English.
Scopus	((TITLE-ABS-KEY(cataract surgery OR cataract extraction OR phacoemulsification)) AND (TITLE-ABS-KEY(endophthalmitis))) AND (retrospective study OR prospective study OR randomised* trial) AND (LIMIT-TO (SRCTYPE,"j")) AND (LIMIT-TO (DOCTYPE,"ar")) AND (LIMIT-TO (PUBYEAR,2021) OR LIMIT-TO (PUBYEAR,2020) OR LIMIT-TO (PUBYEAR,2019) OR LIMIT-TO (PUBYEAR,2018) OR LIMIT-TO (PUBYEAR,2017) OR LIMIT-TO (PUBYEAR,2016) OR LIMIT-TO (PUBYEAR,2015) OR LIMIT-TO (PUBYEAR,2014) OR LIMIT-TO (PUBYEAR,2013) OR LIMIT-TO (PUBYEAR,2012) OR LIMIT-TO (PUBYEAR,2011) OR LIMIT-TO (PUBYEAR,2010) OR LIMIT-TO (PUBYEAR,2009) OR LIMIT-TO (PUBYEAR,2008) OR LIMIT-TO (PUBYEAR,2007) OR LIMIT-TO (PUBYEAR,2006) OR LIMIT-TO (PUBYEAR,2005) OR LIMIT-TO (PUBYEAR,2004) OR LIMIT-TO (PUBYEAR,2003) OR LIMIT-TO (PUBYEAR,2002) OR LIMIT-TO (PUBYEAR,2001) OR LIMIT-TO (PUBYEAR,2000)) AND (LIMIT-TO (LANGUAGE,"English"))

(*e.g.*, immediately sequential bilateral cataract extraction or cataract surgeries combined with other ophthalmological procedures), if the study did not mention the use or non-use of any prophylactic measures against POE, and if the POE incidence was not reported in absolute figures.

Data collation

Data from each study was extracted and compiled in standardized form including: (a) year of publication, (b) country/region, (c) study type, (d) study period, and (e) reported POE incidence in percentage and absolute figures.

Where reported, any prophylactic measure, *i.e.*, IC antibiotics and the corresponding POE incidence (in percentage and absolute figures) was also recorded. In studies that reported the incidence of both presumed POE (diagnosed clinically) and culture-positive POE, the presumed POE incidence was recorded. In studies that reported endophthalmitis complication rates for procedures other than cataract surgeries, only the relevant data (POE following cataract surgery) was recorded. In studies that only provided absolute figures, percentages were calculated.

Statistical analysis

All analysis was performed in IBM SPSS Statistics v.27. Some of the included studies reported POE incidence over a few years, *i.e.*, x% between 2001 and 2005. For these studies, we identified the median year and generated a scatter plot of overall POE incidence (%) against year.

Studies were separated into those that included prophylactic IC antibiotics and those that did not. Within these groups, studies were further separated into studies that only had single data points and studies with multiple data points. Binary logistic regression was performed on the following groups: (A) all studies that involved prophylactic IC antibiotics, (B) all studies that did not involve IC antibiotics, and (C) studies that only had single data points. If a study including IC antibiotics did not provide absolute figures for the breakdown of POE cases in non-IC antibiotic groups *versus* IC antibiotic groups, they were excluded from this analysis.

For group A, a generalized estimating equation with study ID as subject identifier, an exchangeable correlation structure (robust estimator) and a logit link function was used to investigate the effects of prophylactic IC antibiotics on POE incidence. For group B, a generalized estimating equation with study ID as the subject identifier, year fitted as a within subject covariate with an AR(1) autoregressive correlation structure (robust estimator), and a logit link function was used to investigate any time trends associated with POE incidence. For group C, a generalized linear model with a logit link function was used to investigate if there were any time trends associated with POE incidence in this group. Line plots for

groups A and B, and a scatter plot for group C were also generated. Results were considered significant if $p < 0.05$.

Studies from Australia, China, Europe, India, Singapore, and United States were identified, and the pooled POE incidence for each region was calculated to generate a bar chart. These pooled incidence rates were further categorized into POE incidence for patients who did not receive prophylactic IC antibiotics and patients who received IC antibiotics.

Results

Study characteristics

A total of 63 studies were included in our analysis (Table 2). These studies consisted of: eight studies from India,[13–20] eight from Spain,[21–28] eight from United States,[29–36] six from United Kingdom,[37–42] five from Sweden,[43–47] four from Brazil,[48–51] four from Japan,[52–55] three from France,[56–58] two from China,[59,60] two from Greece,[61,62] two from Ireland,[63,64] two from Singapore,[65,66] and a single study each from Australia,[67] Canada,[68] Europe,[5] Germany,[69] Hong Kong,[70] Israel,[71] Portugal,[72] Saudi Arabia,[73] and Taiwan.[74] Thirty-one of these studies included the use of prophylactic IC antibiotics. One study was excluded from the subgroup analysis as it did not report the breakdown of POE cases within groups receiving and not receiving IC antibiotics.[56] Within the remaining thirty, three studies had a single data point. Twenty-seven studies included data points from patients not receiving IC antibiotics; for the purpose of this review, we shall refer to these patients as the 'baseline' groups within those studies.

Table 2. Characteristics of included studies

Study ID	Year	Authors	Country/ region	Study type	Reference
1	2019	Moser *et al.*	Spain	Retrospective observational study	21
2	2019	Haripriya *et al.*	India	Retrospective multicenter clinical registry	13
3	2019	Melega *et al.*	Brazil	Prospective randomized partially masked single-site clinical trial	51
4	2018	Tuñí-Picado *et al.*	Spain	Retrospective comparative study	22

Study ID	Year	Authors	Country/ region	Study type	Reference
5	2018	Inoue *et al.*	Japan	Prospective multi-center study	52
6	2017	Haripriya *et al.*	India	Retrospective clinical registry	14
7	2016	Haripriya *et al.*	India	Retrospective clinical registry	15
8	2016	Herrinton *et al.*	US	Observational, longitudinal cohort study	29
9	2015	Katz *et al.*	Israel	Retrospective consecutive cohort study	71
10	2015	Sharma *et al.*	India	Prospective comparative interventional cohort study	16
11	2015	Rahman N, Murphy CC	Ireland	Retrospective case note review	63
12	2015	Asencio *et al.*	Spain	Retrospective case control study	23
13	2014	Beselga *et al.*	Portugal	Retrospective comparative unicentric institutional study	72
14	2013	Matsuura *et al.*	Japan	Retrospective survey cohort study	53
15	2013	Shorstein *et al.*	US	Retrospective ecological time-trend study	30
16	2012	Haripriya *et al.*	India	Retrospective cohort study	17
17	2010	Wykoff *et al.*	US	Retrospective, consecutive case series	31

Study ID	Year	Authors	Country/ region	Study type	Reference
18	2010	García-Sáenz *et al.*	Spain	Prospective comparative study	24
19	2009	Lloyd JC, Braga-Mele R	Canada	Retrospective, consecutive case series	68
20	2008	Yu-Wai-Man *et al.*	UK	Retrospective analysis	37
21	2007	Endophthalmitis Study Group, European Society of Cataract & Refractive Surgeons	Europe	Prospective randomized partially masked multicenter trial	5
22	2007	Lundström *et al.*	Sweden	Prospective, multicenter, comparative, nonrandomized, observational study	43
23	2007	Moshirfar *et al.*	US	Retrospective, multicenter, observational case series	32
24	2006	Wu *et al.*	Taiwan	Retrospective, comparatice, case-controlled study	74
25	2003	Nagaki *et al.*	Japan	Multicenter study	54
26	2002	Kalpadakis *et al.*	Greece	Retrospective clinical study	61
27	2002	Montan *et al.*	Sweden	Noncontrolled retrospective observational study	44

Study ID	Year	Authors	Country/ region	Study type	Reference
28	2021	Kato *et al.*	Brazil	Retrospective, descriptive, observational study	48
29	2020	Rathi *et al.*	India	Prospective, nonrandomized, comparative, interventional study	18
30	2020	Ma *et al.*	China	Retrospective, comparative, interventional cohort study	59
31	2019	Luz *et al.*	Brazil	Descriptive study of medical records	49
32	2017	Oshika *et al.*	Japan	Prospective case series	55
33	2016	Au *et al.*	Australia	Retrospective longitudinal cohort study	67
34	2016	Creuzot-Garcher *et al.*	France	Cohort study	56
35	2016	Kwok *et al.*	Hong Kong	Retrospective cohort study	70
36	2014	Asencio *et al.*	Spain	Quasi-experimental retrospective study	25
37	2012	Barreau *et al.*	France	Clinical trials	57
38	2012	Romero-Aroca *et al.*	Spain	Prospective, observational study	26
39	2011	Lin *et al.*	China	Retrospective study	60

Study ID	Year	Authors	Country/ region	Study type	Reference
40	2011	Ness *et al.*	Germany	Retrospective clinical study	69
41	2010	Anijeet *et al.*	UK	Retrospective analysis	38
42	2009	Krikonis *et al.*	Greece	Retrospective, observational case series	62
43	2009	Carrim *et al.*	UK	Retrospective consecutive audit	39
44	2009	Al-Mezaine *et al.*	Saudi Arabia	Retrospective observational case series	73
45	2009	Garat *et al.*	Spain	Comparative study	27
46	2008	Kodjikian *et al.*	France	Retrospective cohort study	58
47	2007	Kelly *et al.*	UK	Hospital based retrospective case series	40
48	2007	Mollan *et al.*	UK	Retrospective noncomparative consecutive series	41
49	2006	Patwardhan *et al.*	UK	Single-center study	42
50	2006	Romero *et al.*	Spain	Non-controlled retrospective observational study	28
51	2005	Khan *et al.*	Ireland	Retrospective series	64
52	2005	Wejde *et al.*	Sweden	Prospective survey	45

Study ID	Year	Authors	Country/ region	Study type	Reference
53	2005	Lalitha *et al.*	India	Retrospective, interventional, observational case series	19
54	2005	Jensen *et al.*	US	Retrospective, cross-sectional (prevalence) study	33
55	2004	Buzard K, Liapis S	US	Prospective institutional study	34
56	2004	Wong TY, Chee SP	Singapore	Prospective case series	66
57	2002	Montan *et al.*	Sweden	Prospective survey	46
58	2017	Vieira *et al.*	Brazil	Retrospective clinical registry-based study	50
59	2005	Miller *et al.*	US	Retrospective, observational case series	35
60	2013	Friling *et al.*	Sweden	Prospective epidemiologic study	47
61	2009	Ravindran *et al.*	India	Retrospective observational series	20
62	2015	Schelonka LP, SaBell MA	US	Prospective interventional case series	36
63	2012	Tan *et al.*	Singapore	Cohort study	65

Trends in incidence of POE following cataract surgery

The overall incidence of POE over time was extracted from each of the 63 studies and visually represented as a scatter plot (Fig. 1). The included studies had data points spread over 1993–2017.

For studies with single datapoints, there was evidence of a downward linear trend in the incidence of POE over time (Fig. 2). The risk ratio per year was 0.928, 95% CI [0.911, 0.945], $p < 0.001$. This trend was unchanged when studies using prophylactic IC antibiotics were removed, resulting in a risk ratio of 0.941, 95% CI [0.923,0.959], $p < 0.001$.

A downward linear trend was also observed within studies that had multiple data points and did not utilize any prophylactic IC antibiotics (Fig. 3). The risk ratio per year for these studies was 0.936, 95% CI [0.887, 0.988], $p = 0.017$.

In studies that involved prophylactic IC antibiotics and had multiple data points, the relative risk of POE when no IC antibiotics were used *versus* when IC antibiotics were used was 3.705, 95% CI [3.019,4.547], $p < 0.001$ (Fig. 3). Within these studies, the range of POE incidence in the baseline group was 0.02–1.24%, with a median of 0.29%. The range of POE incidence in patients who received IC antibiotics was 0.00–0.11%, with a median of 0.04%.

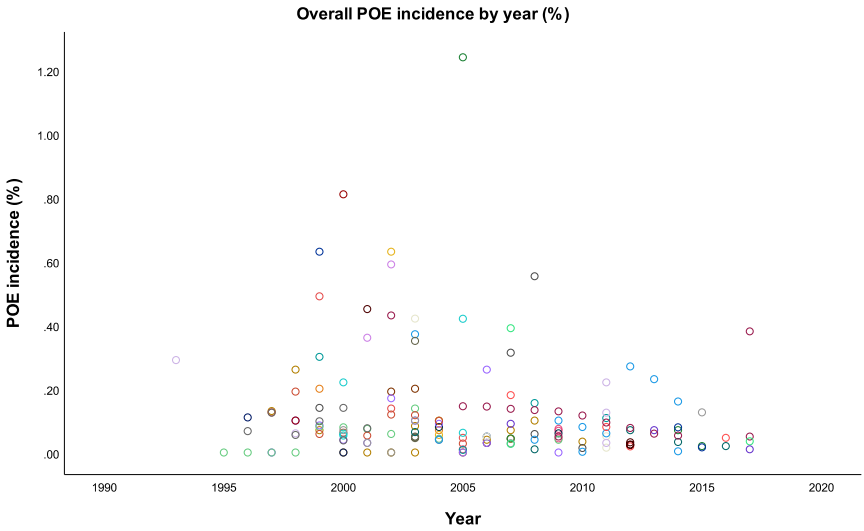

Fig 1. Visual representation of the overall incidence of postoperative endophthalmitis (%) across 1993–2017. Data was collected and compiled from a total of 63 included studies. If studies spanning multiple years did not report annual incidences, the overall incidence was plotted against the median year of the study period.

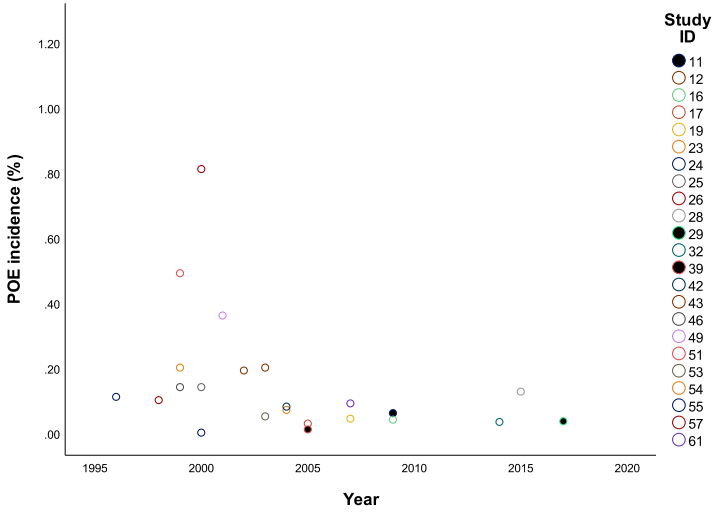

Fig 2. Scatter plot showing postoperative endophthalmitis incidence (%) against year in studies with single datapoints (n = 23). Legend (right) shows the study ID associated with each data point. Studies 11, 29, and 39 (black fill) involved the use of prophylactic intracameral antibiotics.

The overall range of POE incidence in all patients who did not receive IC antibiotics in this review was 0.00–1.24%, with a median of 0.08%. This included patients who were part of studies that did not use any prophylactic IC antibiotics, and the baseline groups in studies that used prophylactic IC antibiotics.

The pooled sample size for each region (Fig. 4) was as follows: India (2,965,980), Europe (1,425,528), United States (215,479), China (155,949), Singapore (94,980), and Australia (14,805). Australia had the highest pooled POE incidence with 0.43% when prophylactic IC antibiotics were not used, followed by Europe (0.20%), Singapore (0.07%), India (0.07%), United States (0.05%), and China (0.03%). When prophylactic IC antibiotics were administered, Australia had the highest POE incidence with 0.05%, then United States (0.04%), Europe (0.04%), India (0.02%), Singapore (0.01%) and China (0.01%).

Discussion

This review shows a downwards trend in POE incidence across 1993–2017 (Figs. 2 and 3). This agrees with current literature describing a perceived drop in POE since the publication of Taban *et al.*'s findings.[75]

Several factors have been proposed to contribute towards this decrease, with one of the most discussed factors being the use of prophylactic IC antibiotics, which has recently become more common in cataract surgeries. In 1998, 75%

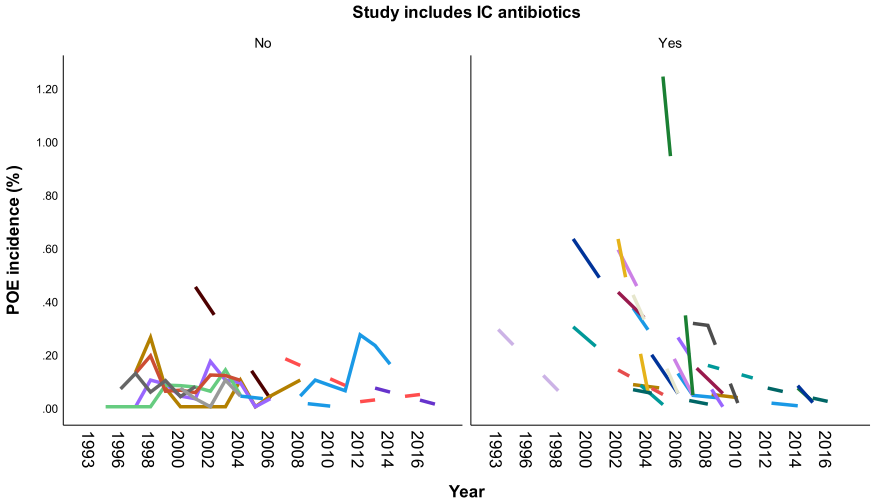

Fig. 3. Line plots showing postoperative endophthalmitis incidence (%) against year in studies with multiple data points, separated into studies including intracameral antibiotic prophylaxis (right; n = 27) and studies not including intracameral antibiotic prophylaxis (left; n = 12).

of Australian ophthalmologists surveyed reported a preference for subconjunctival antibiotics;[76] in 2017, approximately 78.3% of Australian and New Zealand ophthalmologists reported using IC antibiotics.[12] A French study showing a drop in POE incidence from 0.145% to 0.035% attributed the significant reduction to the increased availability of IC cefuroxime injections,[56] and Swedish and Singaporean papers included in this review have identified the non-use of IC antibiotics as a risk factor for POE.[47,65] This review found a significantly reduced risk of POE when IC antibiotics were used: the risk of POE was reduced almost four-fold. Again, our findings are in line with the available literature.[6–8] The median POE incidence in patients that were administered IC antibiotics in our review was 0.04%, which is comparable to the reported average POE rates of 0.03%, 0.02% and 0.01% for IC cefuroxime, moxifloxacin, and vancomycin respectively.[77]

However, it is interesting to note that many of the studies including prophylactic IC antibiotics appear to have high POE rates in their baseline groups (Fig. 3), with the highest reported incidence being 1.24%, which later dropped to 0.04% upon use of prophylactic IC antibiotics.[57] The median POE incidence was 0.29%. In comparison, the median POE incidence in all non-IC antibiotic patients in this review was 0.08%. This is of particular significance, as a common critique of the ESCRS study is that it has a high rate of POE in its control group (0.35%) compared to other studies, and that the perceived benefit of IC antibiotics may therefore be exaggerated.[9] Other concerns surrounding the ESCRS

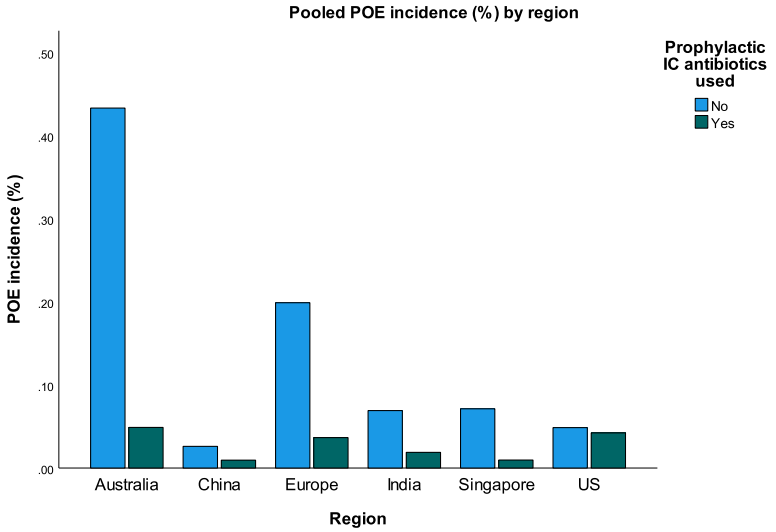

Fig 4. Bar chart of pooled postoperative endophthalmitis (POE) incidence rates (%) by region for the following regions: Australia (n = 1), China (n = 2), Europe (n = 28), India (n = 8), Singapore (n = 2) and US (n = 8). POE incidence was further separated into groups where prophylactic antibiotics were used (green: right) and where they were not used (blue: left).

study include its use of topical levofloxacin instead of fourth-generation fluoroquinolones, the variable surgical techniques causing potential confounding factors, as well as the fact that the study was not blinded for the cefuroxime administration.[3,69,75]

Furthermore, a 2018 Japanese study showed a lower POE incidence of 11/46,741 in eyes not receiving IC antibiotics (0.024%) compared to 2/6,242 eyes receiving IC antibiotics (0.032%). Given the extremely low POE incidence in Japan, the authors felt that routine prophylactic IC antibiotics might be unnecessary.[52] A 2015 study from India that investigated the use of prophylactic IC antibiotics also did not find a significant reduction in POE risk.[16]

The downward linear trend we have reported in our review is significant even when excluding studies that use prophylactic IC antibiotics. This is true for both studies that have single data points (Fig. 2) and studies that have multiple data points (Fig. 3), with both groups having a risk ratio per year of 0.936–0.941. We believe that POE incidence is therefore decreasing worldwide even without the use of prophylactic IC antibiotics, and this could be attributed to multiple factors, *e.g.*, improvement in aseptic techniques, surgical techniques, and surgical equipment.

The pooled POE incidence rates by region allow for some commentary on the differences between each included region (Fig. 4). Australia appears to have the highest POE incidence with and without prophylactic IC antibiotics, as well as the largest reduction in POE rates with IC antibiotics; however, this data is from a single tertiary center in Sydney[67] and has the smallest sample size among all the regions. A 2011 large-scale study of 129,982 patients in Western Australia reported a POE rate of 0.18% between 1980 and 2001,[78] which is lower than the reported rate of 0.43% in the 2016 Australian study included in this review. The 2011 Western Australia study was excluded from this review as it did not describe the use or non-use of prophylactic IC antibiotics.

Europe has the second highest POE incidence without IC antibiotics, and the second largest reduction in POE rates with IC antibiotic administration. The POE incidence of 0.20% is lower than the incidence reported in the 2007 ESCRS control group (0.35%). Interestingly, there is a big difference between Europe's non-IC antibiotic POE incidence and Singapore's non-IC antibiotic POE incidence (0.08%), which is the next highest value. This could be due to the large number of studies ($n = 28$) and heterogeneity of data included in its calculation. The POE incidence with IC antibiotics is comparable with reported values in recent systematic reviews.[77]

The POE incidence for the United States is extremely similar with and without IC antibiotics. This could be related to the relative paucity of IC antibiotic use compared to other regions such as Europe, and therefore a consequent paucity of literature. Studies reporting POE incidence with IC antibiotic use ($n = 2$) were from California and may not be representative of the whole country. These numbers could further explain the ongoing preference for US ophthalmologists to use topical, fourth-generation fluoroquinolones as POE prophylaxis over IC antibiotics. There is currently no FDA-approved antibiotic preparation for IC use in the United States[79] and reconstitution of these antibiotics into preparations for IC use carries a risk of dilutional or dosage errors, which can further increase the risk of toxic anterior shock syndrome.[72] Since studies in the United States that did not use prophylactic IC antibiotics at all ($n = 6$) consistently reported POE rates below 0.05%, the benefit of IC antibiotics is reduced and should be thoroughly weighed against its risks before use. This is similar to Japan, where non-IC antibiotic POE incidence can be lower than POE incidence with IC antibiotics, and where the vast majority of ophthalmologists do not routinely use prophylactic IC antibiotics.

Singapore and India had similar POE rates with and without IC antibiotic prophylaxis, with Singapore having a slightly greater reduction. China had the lowest POE rates both with and without IC antibiotic prophylaxis, although there were only two studies included with a sample size of 155,949, which may not be representative of the whole country.

Limitations

There are several limitations to this review. Firstly, the number of included studies varies between countries and limits our analysis, as some countries are more poorly represented than others. Certain studies that contained large-scale data, *e.g.*, the 2011 Western Australia study and US Medicare studies were excluded as they did not specify the use or non-use of IC antibiotics, which was of interest to us.

Secondly, the heterogeneity of data reporting meant that we had to represent some of the available data differently. While some studies provided an annual breakdown of POE cases and number of cataract surgeries, others only reported the overall number of cases and surgeries across a study period. In order to include them in our analysis, we needed to select a single time point to generate a data point. The nature of this paper is also a limitation: as a review, we are unable to account for the various confounding factors between each paper. It is important to keep this heterogeneity and data collection in mind while interpreting our results.

The continued publication of POE data and prophylactic information in each country is important to understand the natural historical aspect of POE and can also aid in decision-making regarding the use of prophylactic IC antibiotics. A future review that includes more papers and investigates further risk factors for POE would be beneficial in further understanding the time trend of POE incidence.

Conclusion

Our review found that the use of IC antibiotic prophylaxis can reduce POE, and that POE incidence is decreasing worldwide even without the use of prophylactic IC antibiotics. In several studies that purported the benefits of IC antibiotics, the baseline POE incidence in the control groups tended to be higher than the overall worldwide POE incidence.

Our review has also compared the pooled POE incidence between a few different regions. Australia and Europe have the highest rates of POE without IC antibiotics, and the greatest reduction in POE incidence when IC antibiotics are used prophylactically. Singapore, India, and China each had a POE incidence < 0.10% even without prophylactic IC antibiotics, and even lower POE rates after using prophylactic IC antibiotics. United States was the only country to have a POE incidence of 0.04% with a < 0.02% reduction after IC antibiotics use.

While there is evidence for the benefit of IC antibiotics as prophylaxis against POE, we believe that this benefit is most valuable when POE incidence is high. In settings where POE incidence is naturally low, the risks of IC antibiotics could outweigh its benefit. It is therefore important to assess the baseline POE incidence

for each surgical facility thoroughly before implementing the use of IC antibiotics as routine prophylaxis.

Declarations

Ethics approval and consent to participate
Not required.

Consent for publication
Not required.

Competing interests
None to declare.

Funding
None to declare.

Acknowledgements
The authors would like to acknowledge Dr. Karen Byth and Dr. Rachel O'Connell at the NHMRC Clinical Trials Centre within the University of Sydney for their statistical support and guidance.

References
1. Barry P, Cordovés L, Gardner S. ESCRS Guidelines for Prevention and Treatment of Endophthalmitis Following Cataract Surgery: Data, Dilemmas and Conclusions. European Society of Cataract and Refractive Surgeons. 2013. Available from: http://www.escrs.org/downloads/Endophthalmitis-Guidelines.pdf
2. Durand ML. Endophthalmitis. Clin Microbiol Infect. 2013;19(3):227–234.
3. Packer M, Chang DF, Dewey SH, et al. Prevention, diagnosis, and management of acute postoperative bacterial endophthalmitis. J Cataract Refract Surg. 2011;37(9):1699–1714.
4. Taban M, Behrens A, Newcomb RL, et al. Acute endophthalmitis following cataract surgery: a systematic review of the literature. Arch Ophthalmol. 2005;123(5):613–620.
5. Endophthalmitis Study Group, European Society of Cataract & 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(6):978–988.
6. 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 (Copenh). 2015;93(4):303–317.
7. Huang J, Wang X, Chen X, Song Q, Liu W, Lu L. Perioperative Antibiotics to Prevent Acute Endophthalmitis after Ophthalmic Surgery: A Systematic Review and Meta-Analysis. PloS One. 2016;11(11):e0166141.
8. Gower EW, Lindsley K, Tulenko SE, Nanji AA, Leyngold I, McDonnell PJ. Perioperative antibiotics for prevention of acute endophthalmitis after cataract surgery. Cochrane Database Syst Rev. 2017;2:CD006364.
9. Liesegang TJ. Intracameral antibiotics: questions for the United States based on prospective studies. J Cataract Refract Surg. 2008 Mar;34(3):505–509.

10. Lipsky L, Barrett G. Intracameral antibiotics for prophylaxis of postoperative endophthalmitis in Australia: Response. Clin Experiment Ophthalmol. 2020;48(1):139–140.
11. Behndig A, Cochener B, Güell JL, et al. Endophthalmitis prophylaxis in cataract surgery: overview of current practice patterns in 9 European countries. J Cataract Refract Surg. 2013;39(9):1421–1431.
12. Grzybowski A, Schwartz SG, Matsuura K, et al. Endophthalmitis Prophylaxis in Cataract Surgery: Overview of Current Practice Patterns Around the World. Curr Pharm Des. 2017;23(4):565–573.
13. Haripriya A, Chang DF, Ravindran RD. Endophthalmitis reduction with intracameral moxifloxacin in eyes with and without surgical complications: Results from 2 million consecutive cataract surgeries. J Cataract Refract Surg. 2019;45(9):1226–1233.
14. Haripriya A, Chang DF, Ravindran RD. Endophthalmitis Reduction with Intracameral Moxifloxacin Prophylaxis: Analysis of 600 000 Surgeries. Ophthalmology. 2017;124(6):768–775.
15. Haripriya A, Chang DF, Namburar S, Smita A, Ravindran RD. Efficacy of Intracameral Moxifloxacin Endophthalmitis Prophylaxis at Aravind Eye Hospital. Ophthalmology. 2016;123(2):302–308.
16. Sharma S, Sahu SK, Dhillon V, Das S, Rath S. Reevaluating intracameral cefuroxime as a prophylaxis against endophthalmitis after cataract surgery in India. J Cataract Refract Surg. 2015;41(2):393–399.
17. Haripriya A, Chang DF, Reena M, Shekhar M. Complication rates of phacoemulsification and manual small-incision cataract surgery at Aravind Eye Hospital. J Cataract Refract Surg. 2012;38(8):1360–1369.
18. 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(5):819–824.
19. Lalitha P, Rajagopalan J, Prakash K, Ramasamy K, Prajna NV, Srinivasan M. Postcataract Endophthalmitis in South India: Incidence and Outcome. Ophthalmology. 2005;112(11):1884–1889.
20. Ravindran RD, Venkatesh R, Chang DF, Sengupta S, Gyatsho J, Talwar B. Incidence of post-cataract endophthalmitis at Aravind Eye Hospital: Outcomes of more than 42 000 consecutive cases using standardized sterilization and prophylaxis protocols. J Cataract Refract Surg. 2009;35(4):629–636.
21. Moser CL, Lecumberri Lopez M, Garat M, Martín-Baranera M. Prophylactic intracameral cefazolin and postoperative topical moxifloxacin after cataract surgery: endophthalmitis risk reduction and safety results in a 16-year study. Graefes Arch Clin Exp Ophthalmol. 2019;257(10):2185–2191.
22. Tuñí-Picado J, Martínez-Palmer A, Fernández-Sala X, et al. Infectious postoperative endophthalmitis after cataract surgery performed over 7 years. The role of azithromycin versus ciprofloxacin eye drops. Rev Espanola Quimioter. 2018;31(6):15–21.
23. Asencio MA, Huertas M, Carranza R, Tenias JM, Celis J, Gonzalez-Del Valle F. A case-control study of post-operative endophthalmitis diagnosed at a Spanish hospital over a 13-year-period. Epidemiol Infect. 2015;143(1):178–183.
24. García-Sáenz MC, Arias-Puente A, Rodríguez-Caravaca G, Bañuelos JB. Effectiveness of intracameral cefuroxime in preventing endophthalmitis after cataract surgery Ten-year comparative study. J Cataract Refract Surg. 2010;36(2):203–207.
25. Asencio MA, Huertas M, Carranza R, Tenias JM, Celis J, Gonzalez-Del Valle F. Impact of changes in antibiotic prophylaxis on postoperative endophthalmitis in a Spanish hospital. Ophthalmic Epidemiol. 2014;21(1):45–50.
26. Romero-Aroca P, Méndez-Marin I, Salvat-Serra M, Fernández-Ballart J, Almena-Garcia M, Reyes-Torres J. Results at seven years after the use of intracamerular cefazolin as an endophthalmitis prophylaxis in cataract surgery. BMC Ophthalmol. 2012;12(1).

27. Garat M, Moser CL, Martín-Baranera M, Alonso-Tarrés C, Álvarez-Rubio L. Prophylactic intracameral cefazolin after cataract surgery. Endophthalmitis risk reduction and safety results in a 6-year study. J Cataract Refract Surg. 2009;35(4):637–642.
28. Romero P, Méndez I, Salvat M, Fernández J, Almena M. Intracameral cefazolin as prophylaxis against endophthalmitis in cataract surgery. J Cataract Refract Surg. 2006;32(3):438–441.
29. Herrinton LJ, Shorstein NH, Paschal JF, et al. Comparative Effectiveness of Antibiotic Prophylaxis in Cataract Surgery. Ophthalmology. 2016;123(2):287–294.
30. Shorstein NH, Winthrop KL, Herrinton LJ. Decreased postoperative endophthalmitis rate after institution of intracameral antibiotics in a Northern California eye department. J Cataract Refract Surg. 2013;39(1):8–14.
31. Wykoff CC, Parrott MB, Flynn HW, Shi W, Miller D, Alfonso EC. Nosocomial acute-onset postoperative endophthalmitis at a university teaching hospital (2002-2009). Am J Ophthalmol. 2010;150(3):392-398.e2.
32. Moshirfar M, Feiz V, Vitale AT, Wegelin JA, Basavanthappa S, Wolsey DH. Endophthalmitis after uncomplicated cataract surgery with the use of fourth-generation fluoroquinolones: a retrospective observational case series. Ophthalmology. 2007;114(4):686–691.
33. Jensen MK, Fiscella RG, Crandall AS, et al. A retrospective study of endophtalmitis rates comparing quinolone antibiotics. Am J Ophthalmol. 2005;139(1):141–148.
34. Buzard K, Liapis S. Prevention of endophthalmitis. J Cataract Refract Surg. 2004;30(9):1953–1959.
35. Miller JJ, Scott IU, Flynn HW, Smiddy WE, Newton J, Miller D. Acute-onset Endophthalmitis After Cataract Surgery (2000–2004): Incidence, Clinical Settings, and Visual Acuity Outcomes After Treatment. Am J Ophthalmol. 2005;139(6):983–987.
36. Schelonka LP, SaBell MA. Postcataract endophthalmitis prophylaxis using irrigation, incision hydration, and eye pressurization with vancomycin. Clin Ophthalmol. 2015;9:1337–1345.
37. Yu-Wai-Man P, Morgan SJ, Hildreth AJ, Steel DH, Allen D. Efficacy of intracameral and subconjunctival cefuroxime in preventing endophthalmitis after cataract surgery. J Cataract Refract Surg. 2008;34(3):447–451.
38. Anijeet DR, Palimar P, Peckar CO. Intracameral vancomycin following cataract surgery: An eleven-year study. Clin Ophthalmol. 2010;4(1):321–326.
39. Carrim ZI, Richardson J, Wykes WN. Incidence and visual outcome of acute endophthalmitis after cataract surgery - The experience of an eye department in Scotland. Br J Ophthalmol. 2009;93(6):721–725.
40. Kelly SP, Mathews D, Mathews J, Vail A. Reflective consideration of postoperative endophthalmitis as a quality marker. Eye. 2007;21(11):1419–1426.
41. Mollan SP, Gao A, Lockwood A, Durrani OM, Butler L. Postcataract endophthalmitis: Incidence and microbial isolates in a United Kingdom region from 1996 through 2004. J Cataract Refract Surg. 2007;33(2):265–268.
42. Patwardhan A, Rao GP, Saha K, Craig EA. Incidence and outcomes evaluation of endophthalmitis management after phacoemulsification and 3-piece silicone intraocular lens implantation over 6 years in a single eye unit. J Cataract Refract Surg. 2006;32(6):1018–1021.
43. Lundström M, Wejde G, Stenevi U, Thorburn W, Montan P. Endophthalmitis after cataract surgery: a nationwide prospective study evaluating incidence in relation to incision type and location. Ophthalmology. 2007;114(5):866–870.
44. Montan PG, Wejde G, Koranyi G, Rylander M. Prophylactic intracameral cefuroxime. Efficacy in preventing endophthalmitis after cataract surgery. J Cataract Refract Surg. 2002;28(6):977–981.
45. Wejde G, Montan P, Lundström M, Stenevi U, Thorburn W. Endophthalmitis following cataract surgery in Sweden: national prospective survey 1999–2001. Acta Ophthalmol. 2005;83(1):7–10.
46. Montan P, Lundström M, Stenevi U, Thorburn W. Endophthalmitis following cataract surgery in Sweden. The 1998 national prospective survey. Acta Ophthalmol. 2002;80(3):258–261.

47. Friling E, Lundström M, Stenevi U, Montan P. Six-year incidence of endophthalmitis after cataract surgery: Swedish national study. J Cataract Refract Surg. 2013;39(1):15–21.
48. Kato JM, Tanaka T, de Oliveira LMS, et al. Surveillance of post-cataract endophthalmitis at a tertiary referral center: a 10-year critical evaluation. Int J Retina Vitr. 2021;7(1):14.
49. Luz RA, Dall'Oglio LS, Silva FS, Ghirelli W, Padoveze MC. Endophthalmitis after cataract surgery: Results from seven years of epidemiological surveillance. Rev Bras Oftalmol. 2019;78(2):86–90.
50. Vieira IV, Boianovsky C, Saraiva TJ, et al. Safety and efficacy of intracameral moxifloxacin injection for prophylaxis of endophthalmitis after phacoemulsification. Arq Bras Oftalmol. 2017;80(3):165–167.
51. Melega MV, Alves M, Cavalcanti Lira RP, et al. Safety and efficacy of intracameral moxifloxacin for prevention of post-cataract endophthalmitis: Randomized controlled clinical trial. J Cataract Refract Surg. 2019 Mar;45(3):343–350.
52. Inoue T, Uno T, Usui N, et al. Incidence of endophthalmitis and the perioperative practices of cataract surgery in Japan: Japanese Prospective Multicenter Study for Postoperative Endophthalmitis after Cataract Surgery. Jpn J Ophthalmol. 2018;62(1):24–30.
53. Matsuura K, Miyoshi T, Suto C, Akura J, Inoue Y. Efficacy and safety of prophylactic intracameral moxifloxacin injection in Japan. J Cataract Refract Surg. 2013;39(11):1702–1706.
54. Nagaki Y, Hayasaka S, Kadoi C, et al. Bacterial endophthalmitis after small-incision cataract surgery. effect of incision placement and intraocular lens type. J Cataract Refract Surg. 2003;29(1):20–26.
55. Oshika T, Ohashi Y. Endophthalmitis after cataract surgery: Effect of behind-the-lens washout. J Cataract Refract Surg. 2017;43(11):1399–1405.
56. Creuzot-Garcher C, Benzenine E, Mariet A-S, et al. Incidence of Acute Postoperative Endophthalmitis after Cataract Surgery: A Nationwide Study in France from 2005 to 2014. Ophthalmology. 2016;123(7):1414–1420.
57. Barreau G, Mounier M, Marin B, Adenis J-P, Robert P-Y. Intracameral cefuroxime injection at the end of cataract surgery to reduce the incidence of endophthalmitis: French study. J Cataract Refract Surg. 2012;38(8):1370–1375.
58. Kodjikian L, Beby F, Rabilloud M, et al. Influence of intraocular lens material on the development of acute endophthalmitis after cataract surgery? Eye. 2008;22(2):184–193.
59. Ma X, Xie L, Huang Y. Intraoperative cefuroxime irrigation prophylaxis for acute-onset endophthalmitis after phacoemulsification surgery. Infect Drug Resist. 2020;13:1455–1463.
60. Lin M, Zhang W, Liu Y, et al. Nosocomial acute-onset postoperative endophthalmitis at a university teaching hospital in China. J Hosp Infect. 2011;79(4):323–327.
61. Kalpadakis P, Tsinopoulos I, Rudolph G, Schebitz K, Froehlich SJ. A comparison of endophthalmitis after phacoemulsification or extracapsular cataract extraction in a socio-economically deprived environment: a retrospective analysis of 2446 patients. Eur J Ophthalmol. 2002;12(5):395–400.
62. Krikonis TS, Panagiotoglou TD, Tsika C, Alegakis A, Pallikaris IG, Tsilimbaris MK. Endophthalmitis after cataract extraction: Incidence, treatment, and outcome in Crete, Greece, during period 2000-2008. Semin Ophthalmol. 2009;24(6):234–238.
63. Rahman N, Murphy CC. Impact of intracameral cefuroxime on the incidence of postoperative endophthalmitis following cataract surgery in Ireland. Ir J Med Sci. 2015;184(2):395–398.
64. Khan RI, Kennedy S, Barry P. Incidence of presumed postoperative endophthalmitis in Dublin for a 5-year period (1997–2001). J Cataract Refract Surg. 2005;31(8):1575–1581.
65. Tan CSH, Wong HK, Yang FP. Epidemiology of postoperative endophthalmitis in an Asian population: 11-year incidence and effect of intracameral antibiotic agents. J Cataract Refract Surg. 2012;38(3):425–430.
66. Wong TY, Chee S-P. The epidemiology of acute endophthalmitis after cataract surgery in an Asian population. Ophthalmology. 2004;111(4):699–705.

67. Au CPY, White AJR, Healey PR. Efficacy and cost-effectiveness of intracameral vancomycin in reducing postoperative endophthalmitis incidence in Australia. Clin Experiment Ophthalmol. 2016;44(9):803–811.
68. Lloyd JC, Braga-Mele R. Incidence of postoperative endophthalmitis in a high-volume cataract surgicentre in Canada. Can J Ophthalmol. 2009;44(3):288–292.
69. Ness T, Kern WV, Frank U, Reinhard T. Postoperative nosocomial endophthalmitis: Is perioperative antibiotic prophylaxis advisable? A single centre's experience. J Hosp Infect. 2011;78(2):138–142.
70. Kwok RPW, Yip WWK, Jhanji V, Chan VCK, Young AL. The incidence of postoperative endophthalmitis before and after a revised preoperative surgical site preparation protocol. Asia-Pac J Ophthalmol. 2016;5(2):110–114.
71. Katz G, Blum S, Leeva O, et al. Intracameral cefuroxime and the incidence of post-cataract endophthalmitis: an Israeli experience. Graefes Arch Clin Exp Ophthalmol. 2015;253(10):1729–1733.
72. Beselga D, Campos A, Castro M, et al. Postcataract surgery endophthalmitis after introduction of the ESCRS protocol: a 5-year study. Eur J Ophthalmol. 2014;24(4):516–519.
73. Al-Mezaine HS, Kangave D, Al-Assiri A, Al-Rajhi AA. Acute-onset nosocomial endophthalmitis after cataract surgery. Incidence, clinical features, causative organisms, and visual outcomes. J Cataract Refract Surg. 2009;35(4):643–649.
74. Wu PC, Li M, Chang 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.
75. Schwartz SG, Flynn HW, Grzybowski A, Relhan N, Ferris FL. Intracameral Antibiotics and Cataract Surgery: Endophthalmitis Rates, Costs, and Stewardship. Ophthalmology. 2016;123(7):1411–1413.
76. Morlet N, Gatus B, Coroneo M. Patterns of peri-operative prophylaxis for cataract surgery: a survey of Australian ophthalmologists. Aust NZ J Ophthalmol. 1998;26:5-12.
77. Bowen RC, Zhou AX, Bondalapati S, et al. Comparative analysis of the safety and efficacy of intracameral cefuroxime, moxifloxacin and vancomycin at the end of cataract surgery: a meta-analysis. Br J Ophthalmol. 2018;102(9):1268–1276.
78. Clark A, Morlet N, Ng JQ, Preen DB, Semmens JB. Whole Population Trends in Complications of Cataract Surgery over 22 Years in Western Australia. Ophthalmology. 2011;118(6):1055–1061.
79. Javitt JC. Intracameral Antibiotics Reduce the Risk of Endophthalmitis after Cataract Surgery: Does the Preponderance of the Evidence Mandate a Global Change in Practice? Ophthalmology. 2016;123(2):226–231.