Cataract surgery is one of the most commonly performed surgeries in the world and also one of the safest. However, as with any surgical procedure, complications can occur. Although rare, these complications can be serious and may cause irreversible vision loss.

As the population ages and the rates of cataract surgery increase, surgeons must continue to strive to deliver the most optimal and safest outcomes possible. In my opinion, this entails the use of intraocular antibiotics.

RATIONALE FOR ADOPTION

Endophthalmitis is likely the most feared complication of cataract surgery. A variety of prophylactic measures have been developed for endophthalmitis, targeted against the various sources of infection. Recently, there has been a push by surgeons to use intracameral (IC) antibiotics at the end of phacoemulsification as a result of overwhelming data showing their efficacy in reducing endophthalmitis. These data are so strong, in fact, that many surgeons are abandoning the use of postoperative topical fluoroquinolone drops, which have been considered the gold standard for years, along with preoperative povidone-iodine wash. Although I believe that the benefits of IC are undeniable, I think there are several risks to adopting a purely dropless regimen devoid of postoperative topical antibiotic prophylaxis.

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risk of endophthalmitis is real, as is its sight-threatening potential.

Given the severity of the potential complications, I use IC antibiotics in all cataract surgery cases, unless contraindicated by allergy. This approach is supported by an overwhelming quantity of literature showing the effectiveness of IC antibiotics for endophthalmitis prophylaxis. Key findings from a few significant studies are summarized below.

**ESCRS.** In 2007, the ESCRS Endophthalmitis Study Group published a landmark study on the effects of antibiotic prophylaxis on the incidence of endophthalmitis after cataract surgery. The prospective, randomized clinical trial included nearly 14,000 patients from 24 centers in nine European countries. Investigators evaluated the effects of an IC injection of 1.0 mg cefuroxime at the close of surgery and of an intensive pulsed perioperative topical application of levofloxacin in a 2 X 2 factorial design. A total of 29 patients presented with endophthalmitis, of whom 20 were classified as having proven infective endophthalmitis. The study authors concluded that the absence of an IC cefuroxime prophylactic regimen was associated with a 4.92-fold increase (95% CI, 1.87–12.9) in the risk for total postoperative endophthalmitis. Topical levofloxacin had no statistically significant effect. In a 2013 followup to the ESCRS study, investigators found zero cases of endophthalmitis out of 13,390 cataract surgeries performed using IC cefuroxime.

**Kaiser.** In 2013, investigators at Kaiser Permanente in California set out to evaluate postcataract-surgery rates of endophthalmitis in relation to changing practice patterns in antibiotic administration. They looked at three distinct time periods: (1) 2007, when patients primarily received postoperative antibiotic drops without IC injection; (2) 2008 and 2009, when, in addition to surgeons’ usual postoperative topical drop regimen, patients received IC cefuroxime unless contraindicated; and (3) 2010 and 2011, when all patients received IC injection of cefuroxime, moxifloxacin, or vancomycin while topical antibiotics were used according to surgeon preference. The investigators also evaluated consecutive patients without posterior capsular rupture (PCR) from a subgroup of three surgeons who used IC antibiotics alone without topical antibiotics.

A total of 19 cases of endophthalmitis occurred in 16,264 cataract surgeries. The respective rates per 1,000 during the three time periods were: 3.13 (95% CI, 1.43–5.93) in 2007, 1.43 (95% CI, 0.66–2.72) in 2008 and 2009, and 0.14 (95% CI, 0.00–0.78) in 2010 and 2011.

One case of endophthalmitis was observed in the 2,083 patients who received IC injection only (rate per 1,000: 0.49; 95% CI, 0.01–2.73). The rate of endophthalmitis in 2007 was 0.32%, which was similar to the 0.35% observed in the control group of the ESCRS study.

**Aravind.** In 2017, investigators published the results of a study including 617,453 cataract surgeries performed from January 2014 to May 2016 at 10 Aravind Eye Hospitals in India. Endophthalmitis rates before and after initiation of IC moxifloxacin were statistically compared for all eyes and separately for phacoemulsification and manual small-incision cataract surgery (M-SICS) eyes and for eyes with PCR.

Overall, 314,638 eyes received IC moxifloxacin and 302,815 eyes did not. There was a significant decline in the endophthalmitis rate with IC moxifloxacin, from 0.07% to 0.02%. For the 194,252 phaco eyes, the endophthalmitis rate was 0.07%
FACE-OFF

without IC moxifloxacin prophylaxis, compared with 0.01% with IC moxi-
floxacin. For the 414,657 M-SICS eyes, the endophthalmitis rate was 0.07%
without IC moxifloxacin and 0.02% with moxifloxacin. Approximately
half of the 8,479 eyes with PCR received IC moxifloxacin and half
did not. Without IC moxifloxacin, PCR increased the endophthalmitis
rate nearly sevenfold, to 0.48%; in contrast, IC moxifloxacin reduced the
endophthalmitis rate with PCR to 0.21%.

The investigators concluded that routine IC moxifloxacin prophylaxis
reduced the overall rate of endo-

phthalmitis by 3.5-fold (threelfold for
M-SICS and nearly sixfold for phaco-
emulsification), and they noted that IC antibiotics had a significant ben-

efit for eyes with PCR.

Bowen. A recent meta-analysis
by Bowen and colleagues’ pooled
data from 17 studies published over
the past 2 decades. Apart from the
ESCRS randomized clinical trial, all
were observational studies. When
pooled, more than 900,000 eyes
could be analyzed.

Key takeaways from the meta-anal-
ysis include: (1) in terms of volume
of studies and volume of patients, IC
cefuroxime has the greatest support
in the literature and vancomycin the
least; (2) of cefuroxime, moxifloxacin,
and vancomycin, cefuroxime was the
least effective agent, although it was
more efficacious than topical drops;
(3) moxifloxacin was more effective
than cefuroxime and was associated
with less toxicity; (4) most effective
of the three agents was vancomycin,
although it has been associated with
hemorrhagic occlusive retinal vascu-

lus; and (5) topical medications did
not appear to be of benefit.

Bowen et al concluded that
“[IC] cefuroxime and moxifloxacin
reduced endophthalmitis rates com-
pared with controls, with minimal
or no toxicity events at standard
doses. Additionally [IC] antibiotics
alone may be as effective as [IC] plus
topical antibiotics.”

CLEARING HURDLES

Despite mounting evidence that
routine prophylaxis with IC anti-
biotics reduces the rate of endo-

phthalmitis after cataract surgery,
surgeons—particularly those in the
United States—have been slow to
adopt this approach. The reasons
for this are multiple, but not always
sound.

Resistance to change. Humans
have a natural resistance to change.
In 2008, Peter Barry, MD, FRCSC,
chair of the 2007 ESCRs study, noted,
“When our results came out, we were
the subject of robust challenge and
debates in many roundtables and
numerous discussions.” More than a
decade later, the controversies
remain. However, as ophthalmologists
have learned before (eg, phacoemul-
sification), doing something a certain
way simply because that’s how it’s
always been done is insufficient and a
disservice to patients.

Some ophthalmologists may feel
more comfortable with their standard
regimen of administering preopera-
tive povidone-iodine and postopera-
tive topical antibiotics than with an
IC approach. However, have you ever
seen patients administer eye drops?
Enough said.

Safety concerns. The reluctance
to adopt IC antibiotics stems largely
from the commercial unavailability
of a single, sterile, FDA-approved unit
dose for cataract surgery. However,
designing a clinical trial large enough
to show a reduction in a relatively
rare condition is cost-prohibitive.
A 2013 Cochrane review stated, “It
is unlikely that additional clinical
trials will be conducted to evalu-
ate currently available prophylaxis.
Practitioners should rely on current
evidence to make informed decisions
regarding prophylaxis choices.” As
outlined above, the evidence in sup-
port of the use of IC antibiotics is
overwhelming.

Financial disincentive. The lack
of reimbursement for IC antibiotics
is another major barrier to adop-
tion. There is currently no mecha-
nism to pay for the intraoperative
use of a medication to prevent
postoperative drops, even though
it could save the system millions
of dollars. IC moxifloxacin is more
cost-effective than topical administra-
tion based on the cost of the drug
and the money saved by preventing
endophthalmitis. A 3-mL bottle of
moxifloxacin is $153.30. One 3-mL
bottle of moxifloxacin can be split
up 20 times for IC injection, making
the cost per patient $7.67. For those
who would like a commercial option
from a 503B compounding pharmacy,
moxifloxacin is available for $15
(www.imprimisrx.com). Additionally,
many 503A compounding pharmacies
will prepare patient-specific formul-
ations (www.ocularscience.com).

LESSONS LEARNED

As with any surgical approach,
there are hurdles to overcome.
Initially, when I was injecting antibiot-
ics into the vitreous, I was concerned
about disturbing the vitreous, espe-
cially in high myopes. But now that
I inject a combination antibiotic,
steroid, and NSAID into the ante-
rior chamber and subconjunctivally,
those concerns have been alleviated.
Further, I ensure the highest quality
by using IC antibiotics supplied by a
503B compounding pharmacy.

As both surgeon and patient
expectations of cataract surgery con-
tinue to increase, we cannot discount
the significance of a potential com-
plication such as endophthalmitis,
regardless of its incidence in our ORs.
The best outcomes mandate the
best practices, which is why I utilize
IC antibiotics.

1. Gallaghy HE, Hodge DO, St Sauver JL, Erie JC. Increasing incidence
2. Braga-Mele R, Chang DF, Henderson BA, Mamalis N, Talley-Rostov A, for
A recent study examined various endophthalmitis prophylaxis regimens in use around the world and found that there is no global consensus regarding endophthalmitis prophylaxis with cataract surgery, as several studies have shown clinical benefits with different regimens. On one hand, two well-known studies, the ESCRs study and the Kaiser study, both showed a reduced incidence of post-operative endophthalmitis with routine prophylaxis using IC antibiotics. These studies included 14,000 patients and more than 16,000 patients, respectively. On the other hand, a recent study by Rudinsky et al involving 75,318 eyes undergoing cataract surgery in Canada over an 8-year period demonstrated that there was no difference in the rate of endophthalmitis with or without IC prophylaxis. The study did conclude, however, that the incidence of endophthalmitis was lower if a fluoroquinolone was used after surgery.

Additionally, a large study by Lloyd and Braga-Mele including 13,000 eyes undergoing cataract surgery at one institute in Canada over a 2-year period showed postoperative endophthalmitis rates of 0.04%, despite no use of IC antibiotics. This incidence compares favorably to the IC data published in the ESCRs and Kaiser studies, which showed incidences of postoperative endophthalmitis of 0.32% and 0.35%, respectively, for the control groups. Further, the Lloyd and Braga-Mele study also found that more patients developed endophthalmitis if they did not receive postoperative fluoroquinolones.

Although the use of IC is on the rise in the United States, 98% of surgeons reportedly still use prophylactic topical antibiotics. Although clearly there is no consensus on the exact best prophylactic regimen for endophthalmitis, I believe the evidence is clear that both IC and topical antibiotics play a role in helping protect patients from this potentially catastrophic outcome.

Most cases of endophthalmitis result from the seeding of organisms into the anterior chamber at surgery or in the immediate postoperative period; therefore, it makes sense that the injection of a powerful antibiotic into the anterior chamber would reduce potential bacterial load. However, this is complicated by a number of practical problems.

First, there is no FDA-approved class of antibiotics for IC prophylaxis of endophthalmitis. Second, in the United States, there is no approved, uniform, commercially produced, single-use, sterile product available that could even be used. This leaves the cataract surgeon in the unenviable position of relying on either a compounding laboratory to produce an antibiotic for IC injection or having to use commercially available drops (such as moxifloxacin) and to divide and dilute it themselves under sterile conditions (or, more likely and worse yet, someone else on the surgery team with no supervision from the surgeon) on the day of surgery.

Third, we know that some clear corneal cataract wounds remain unstable in the week following surgery, and this can potentially lead to pathogens entering the eye several days later. We also know there is a high rate of aqueous humor turnover in the anterior chamber, and, with the pure IC approach, there would be little drug left in the anterior chamber after 24 hours. Fourth, even with injection into the vitreous cavity, it is important to note that moxifloxacin, the most commonly used antibiotic in the dropless approach, is highly lipophilic and has a very short half-life of less than 2 hours in the vitreous cavity.

A recent study by Kishore et al included roughly 2,000 eyes undergoing cataract surgery over a 15-month period. The study authors concluded that, after as little as 14 hours, “the dropless approach may not provide adequate prophylaxis against susceptible organisms through the period when the eye is at risk.” Given this, what surgeon wouldn’t want a daily topical antibiotic in his or her own eye after cataract surgery to combat the rare (but real) possibility of delayed bacterial migration into the anterior chamber, which would then be devoid of antibiotic coverage with a pure IC approach? Not for my eye.

Still a personal decision

It is doubtful that industry will take on the daunting expenditure of time and money needed to develop an FDA-approved antibiotic for single-use IC injection for postcataract-surgery prophylaxis of endophthalmitis. A
Cochrane review on the subject concluded that “The practitioner should rely on current evidence to make informed decisions regarding prophylaxis choices in cataract surgery.” Translation: Do what you think is right and cross your fingers—not much help. Imagine that courtroom scenario: “Dr. Williamson, you put a needle in Mrs. Smith’s eye and injected a drug that wasn’t approved by the FDA for this indication, and now she’s lost vision? Further, you didn’t use any antibiotic drops postoperatively, which is the gold standard?” To which I’d reply, “Well, yes, but there are some great studies out of Europe and India showing that this works!” Who is to say how a jury may vote, but I don’t want to find out.

It seems that the use of povidone-iodine sterilization and topical antibiotics will continue to be the mainstay for prophylaxis of endophthalmitis, while IC approaches will continue to garner widespread acceptance, as they should, given the data. The efficacy of IC use will continue to be compelling, especially in high-risk patients such as those with PCR, who have a 14-fold increased risk of endophthalmitis. However, I believe the routine use of IC in place of topical antibiotics in every case will remain problematic. We know that the most commonly isolated organisms in endophthalmitis are coagulase-negative staphylococci, which have a reported high resistance to moxifloxacin. So the plan is to inject moxifloxacin into 99.9% of patients who would never have gotten endophthalmitis anyway to protect the 0.1%? If this scenario plays out, the eventuality of super-resistant strains is concerning.

Personally, I have decided to adopt IC antibiotics, but it wasn’t without considerable thought and research, and I certainly will not abandon topical prophylaxis; I will use both for the reasons provided above and will have ironclad informed consent from all patients receiving IC antibiotics.

Surgeons will have to decide for themselves whether they are willing to trust a compounder or to take on the task of producing a single-unit, sterile-use, antibiotic for off-label use in IC injection for every cataract patient. They must also consider the unintended consequences of exposing millions of cataract patients who would never have developed endophthalmitis to the additional potential complications of IC drug use, whether from inflammation, allergy to the drug itself, complications with the actual injection, potential problems with compounding or sterile production of the drug by the surgeon, etc. It could be a daunting task practically and medicolegally on a large scale.


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