

INTRACAMERAL THERAPEUTICS FOR CATARACT SURGERY



Closing in on no-drop surgery.

BY MARK A. KONTOS, MD; AND KENDALL E. DONALDSON, MD, MS

DEXAMETHASONE INTRACAMERAL DRUG-DELIVERY SUSPENSION FOR INFLAMMATION ASSOCIATED WITH CATARACT SURGERY: A RANDOMIZED, PLACEBO-CONTROLLED PHASE III TRIAL

Donnenfeld E, Holland E¹

ABSTRACT SUMMARY

In this randomized, double-masked, placebo-controlled study, investigators sought to determine the safety and efficacy of dexamethasone intraocular suspension 9% (Dexycu, EyePoint Pharmaceuticals) for intracameral administration in two dosages in patients undergoing cataract surgery. Three hundred

ninety-four patients scheduled for cataract surgery at 27 sites were randomly assigned to three groups. Group 1 received a 5- μ L injection of placebo. Groups 2 and 3, respectively, received a 5- μ L injection of 342 μ g or 517 μ g dexamethasone drug delivery suspension into the anterior chamber at the conclusion of cataract surgery. Patients were observed for 90 days after surgery.

The primary outcome measure was anterior chamber cell clearing at postoperative day 8. Secondary measures were anterior chamber flare and anterior chamber cell plus flare clearing in the study eyes. Adverse events were also assessed.

Anterior chamber cell clearing at day 8 was achieved in 25% of eyes in group 1, 63% in group 2, and 66% in group 3 ($P > .001$). Anterior chamber flare clearing at day 8 was achieved in 63.8% of eyes in group 1, 92.4% in group 2, and 89.1% in group 3 ($P > .001$). Adverse events were similar among the three groups with no serious adverse events reported up to postoperative day 90.

DISCUSSION

The appropriate postoperative medical regimen for cataract surgery remains a hotly debated subject. The use of topical steroids alone and in combination continues to be the mainstay of managing inflammation and pain after surgery.^{2,3} Currently the only FDA-approved topical corticosteroids for postoperative inflammation are difluprednate and rimexolone,^{4,5} but topical dexamethasone and prednisolone acetate are commonly used off-label.⁶

Many issues make topical therapy problematic for the treatment of inflammation after cataract surgery. Poor compliance is a major issue. Many patients are unable to administer drops in a consistent manner, making it difficult to know what is actually reaching the eye.⁷ The high cost of medications is another obstacle to proper dosing for some patients. Additionally, adverse events such as IOP spikes and allergic

STUDY IN BRIEF

- A phase 3 clinical trial was designed to determine the safety and efficacy of a novel formulation of intracameral dexamethasone for the treatment of inflammation after cataract surgery. This large multicenter randomized controlled study found that a slow-release delivery system of the drug was a safe and effective alternative to topical steroid therapy after cataract surgery.

WHY IT MATTERS

The possibility of administering a single dose of a steroid at the time of cataract surgery and eliminating postoperative eye drops could offer significant advantages to both surgeons and patients. Based on this study's results, a slow-release delivery system of dexamethasone may help make that possibility a reality. Direct comparisons of this system and other forms of treatment are needed.

reactions make topical therapy less than ideal for the treatment of postoperative inflammation. Eliminating the need for eye drops after cataract surgery could thus offer many advantages.

This study found that intracameral delivery of dexamethasone in a slow-release form can be an effective alternative to topical therapy. The injected 5- μ L droplet forms a sphere

through surface tension in the anterior chamber and slowly releases dexamethasone over a 21-day period. Concentrations are highest on day 1 and steadily decrease thereafter. Patients receiving intracameral dexamethasone showed significantly greater clearing of cell and flare of the anterior chamber compared to the placebo group. This difference was statistically significant

at all endpoints. It was also noted that these patients showed better clearing of the anterior chamber at day 8 than is commonly observed with current topical steroid therapies.⁸ In addition to meeting efficacy endpoints, intracameral dexamethasone was shown to be safe, with no significant adverse events noted during the 90-day period of observation.

SAFETY AND EFFICACY OF INTRACAMERAL MOXIFLOXACIN FOR PREVENTION OF POST-CATARACT ENDOPTHALMITIS: RANDOMIZED CONTROLLED CLINICAL TRIAL

Melega MV, Alves M, Cavalcanti Lira RP, et al⁹

ABSTRACT SUMMARY

This controlled, randomized, single-center (including three hospitals associated with the University of Campinas in São Paulo, Brazil) clinical trial comprised 3,640 eyes of 3,640 patients undergoing cataract surgery. Patients were randomly assigned to one of two groups: one group received an intracameral injection of 0.03 mL (150 μ g) of undiluted moxifloxacin at the end of surgery, and the other received no intracameral injection. All patients received postoperative antibiotic and antiinflammatory drops (0.5% moxifloxacin and 0.1% dexamethasone).

Patients were observed for a period of 6 weeks postoperatively. During this time, the incidence of endophthalmitis was 0.05% (1:1,818 eyes) in the moxifloxacin group and 0.38% (7:1,822 eyes) in the control group ($P = .202$). No side effects related to intracameral moxifloxacin were observed during the study.

DISCUSSION

Since the 2007 publication of ESCRS study results indicating an

overwhelming efficacy of intracameral antibiotics, this practice has gained widespread attention.¹⁰⁻¹³ The ESCRS investigators reported a fivefold decrease in the incidence of endophthalmitis associated with intracameral cefuroxime, resulting in the commercial manufacture of a single-use preparation of this agent labeled for intraocular use (Aprokam, Laboratoires Théa) that quickly became available for use in Europe and elsewhere in the world but not in the United States.¹⁰

This country has faced challenges related to implementation of such a regimen, including issues related to the safety of compounding medications for intraocular use.¹⁴⁻¹⁶ There have been documented cases of compounding errors, including dilutional mistakes, pH imbalance, contamination, and other deviations that have led to profound vision loss in some patients and even loss of

an eye in rare instances.¹⁴⁻¹⁶ Limited availability of intracameral antibiotics globally has prompted many surgeons to prepare drugs in the OR, which has led to errors that have resulted in clinical manifestations such as macular edema, retinal vascular leakage, uveitis, endothelial toxicity, toxic anterior segment syndrome, and infection.¹⁴⁻¹⁶

Moxifloxacin is a fourth-generation fluoroquinolone that provides broad-spectrum coverage against gram-positive bacteria, gram-negative bacteria, atypical microorganisms, and anaerobes. Concern is rising about increasing drug resistance, however, because of moxifloxacin's popularity.¹⁷ The agent has been used off-label for the prevention of endophthalmitis for many years, but only recently has attention begun to focus on conducting controlled trials to better elucidate the drug's efficacy for endophthalmitis prophylaxis.

STUDY IN BRIEF

- ▶ This is the first large prospective randomized controlled clinical trial to evaluate the safety and efficacy of intracameral moxifloxacin for the postoperative prevention of endophthalmitis associated with cataract surgery.

WHY IT MATTERS

Intracameral antibiotics appear to be a safe and effective means of protecting patients from the rare incidence of infection that may be associated with cataract surgery.

As cataract surgery evolves and interest in bilateral, same-day, office-based, no-drop surgery grows, intracameral antibiotics may eventually become a necessity. In the United States, the controlled delivery and manufacturing of these medications are being fine-tuned. ■

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