

THE LITERATURE



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EVALUATION OF SAFETY AND EFFICACY OF SUSTAINED-RELEASE DEXAMETHASONE AFTER CATARACT SURGERY FOR THE TREATMENT OF POSTOPERATIVE INFLAMMATION AND PAIN: MULTICENTER PHASE 3A STUDY

Bafna S, Walters T, Levenson J, et al¹

ABSTRACT SUMMARY

Bafna et al evaluated the safety and efficacy of sustained-release dexamethasone (OTX-DP; Ocular Therapeutix) placed in the canaliculus of the eyelid for the postoperative treatment of ocular inflammation and pain after cataract surgery. This prospective, multicenter, randomized, parallel-arm, double-masked, vehicle-controlled study included 285 subjects randomized unilaterally at 16 sites in the United States.

Patients were randomized 2:1 to receive dexamethasone 0.4 mg or a placebo vehicle punctum plug with no active drug. The investigators performed postoperative evaluations on days 2, 4, 8, 14, 30, 60, and 120 if the test article was confirmed to be present on day 60. The primary endpoints included the absence of anterior chamber cells (score = 0) on day 14 and the absence of pain (score = 0) on day 8. In addition, patients were monitored for the duration of drug delivery over approximately 30 days.

The study found that sustained-release dexamethasone was significantly superior to placebo for the absence of ocular pain on day 8 (80.4% vs 43.4%; $P < .0001$) and for the absence of anterior chamber cells on day 14 (33.1% vs 14.5%; $P = .0018$). Results at other follow-up visits showed efficacy as early as day 2 for ocular pain and day 14 for the absence of anterior chamber cells. No patient in either arm of the study had an increase in IOP over 10 mm Hg from baseline after the day 1 follow-up visit. The investigators did not observe any serious adverse events related to the drug, and no patients lost lines of BCVA during the follow-up period.

DISCUSSION

Approximately 3.5 million cataract surgeries are performed annually in the United States.² Whether used “on” or “off label,” topical corticosteroids, topical nonsteroidal anti-inflammatory drugs (NSAIDs), and topical antibiotic eye drops have become the standard of care for pre- and postoperative treatment.

Unlike glaucoma patients, many cataract patients have little to no experience administering eye drops for themselves or family members. In 2014, An et al found that 92.6% of patients

improperly administered eye drops after cataract surgery.³ The most common reasons included missing the eye, instilling an incorrect amount of drops, contaminating the bottle tip, or failing to wash their hands before instillation. Of the patients who reported never missing their eye, 35% missed under observation, and 57% of those still believed they had instilled the eye drop correctly.

With difficulties resulting from noncompliance, cost, and limitations of topical drug delivery, more and more ophthalmologists are looking for alternatives to eye drops to control postoperative inflammation and prevent infection after cataract surgery.

For the purposes of an FDA study, only one sustained-release drug has been evaluated at a time. Cataract surgeons would like to control postoperative inflammation and pain and also to minimize the potentially devastating effects of postoperative infection. Ocular Therapeutix has completed phase 1 studies of a moxifloxacin punctum plug after cataract surgery (data on file with Ocular Therapeutix). Preliminary results showed that moxifloxacin punctal plugs exhibited 100% retention through day 10 and maintained tear fluid levels above the minimum inhibitory concentration required to inhibit the growth of 90% of common susceptible pathogens for 10 days. Similar to the dexamethasone plug, no adverse events, endophthalmitis, or patient complaints were reported in this study.

The glaucoma adherence and persistency study (GAPS) found adherence to initial glaucoma medication was very



AT A GLANCE

- Bafna et al found that sustained-release dexamethasone was significantly superior to placebo for postoperative pain and inflammation after cataract surgery.¹
- Lewis reported a rate of 2% for CME after the instillation of intracameral triamcinolone and moxifloxacin.⁶
- Advantages of intracameral injections include direct drug delivery into the eye without the need for prodrug vehicles or chemical modifications of the drug molecule and the use of smaller drug amounts, which could reduce the risk of side effects such as IOP elevation. There is also the potential for significant improvement in patients' compliance.

poor and that up to 50% of glaucoma patients stopped taking their medications after 6 months.⁴

Ocular Therapeutix is also developing a sustained-release travoprost punctal plug (OTX -TP) to deliver glaucoma medication to the ocular surface for up to 90 days after instillation.⁵ Further studies are needed to determine whether the pharmacokinetics of punctal plug drug delivery are maintained at adequate levels compared with eye drop therapy. Moreover, patients with small or anomalous tear drainage anatomy may not be candidates for such technology.

MACULAR EDEMA FOLLOWING INTRAVITREAL TRIAMCINOLONE AS AN ALTERNATIVE TO POST-CATARACT ANTIINFLAMMATORY DROPS

Lewis J⁶

ABSTRACT SUMMARY

Lewis retrospectively analyzed 200 consecutive cataract procedures of 129 patients without preexisting macular pathology. The patients were preoperatively imaged with retinal optical coherence tomography on day 1 and at 1 week, 1 month, and 2 months after uncomplicated cataract surgery. After IOL implantation and before viscoelastic removal, Lewis administered a transzonular instillation of 0.2 mL of compounded triamcinolone and moxifloxacin (Tri-Moxi; Imprimis). The central foveal thickness was recorded at all postoperative time intervals.

According to the study, four eyes of two patients developed cystoid macular edema (CME) that resolved with topical steroids and NSAIDs alone. Ten other eyes required postoperative steroids for inflammation without an associated increase in central foveal thickness or visual acuity loss. None of the patients lost lines of BCVA or presented with other adverse side effects, including endophthalmitis.

The author concluded that a rate of 2% CME using intracameral triamcinolone and moxifloxacin was in line with or lower than previous literature reports of CME rates between 0% and 8% after uncomplicated cataract surgery when postoperative topical steroids and NSAIDs were used for up to 8 weeks.

DISCUSSION

Topical eye drop administration has posed many barriers for both patients and health care providers over the past several decades. Among them are the aforementioned high rates of medication noncompliance, excessive branded drug costs, pharmacy-initiated substitutions, increased generic drug prices, uncertain bioavailability, topical toxicity, and a reduction in branded pharmaceutical samples.

As such, dropless cataract surgery has been increasingly used as an alternative to topical medications. Intracameral injections deliver drugs directly into the eye without the

need for prodrug vehicles or chemical modifications of the drug molecule. Other intracameral advantages may include the use of smaller drug amounts, which could reduce the risk of side effects such as IOP elevation.⁷

The European Society of Cataract and Refractive Surgeons Endophthalmitis Study, and more recently, a Northern California Kaiser Permanente Study of 16,264 cataract patients showed a several- to 22-fold decrease in endophthalmitis rates when an antibiotic was administered intracamerally versus topically.^{8,9} At the 2015 Annual Meeting of the American Society of Cataract and Refractive Surgery in San Diego, Galloway reported that intracameral injections of triamcinolone and moxifloxacin in 2,300 sequential cataract surgeries did not result in a single episode of a steroid-induced IOP rise or endophthalmitis postoperatively.¹⁰

Intracameral medication delivery challenges surgeons' learning curves for administration. There is also the issue of cost (and who is to pay for it) along with the use of compounded medications in several state-controlled ambulatory surgery centers. When patients' compliance and safety are considered, however, dropless alternatives or adjuncts to topical therapy may need to play a larger role in cataract surgery. ■

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- financial disclosure: none acknowledged