ARTICLE

Comparison of prednisolone acetate 1.0% and difluprednate ophthalmic emulsion 0.05% after cataract surgery: Incidence of postoperative steroid-induced ocular hypertension

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Purpose: To compare intraocular pressure (IOP) outcomes between 2 common, commercially available corticosteroid drops: difluprednate ophthalmic emulsion 0.05% and prednisolone acetate 1.0%.

Setting: TLC Eyecare and Laser Centers, Jackson, Michigan, USA.

Design: Retrospective chart review.

Methods: The outcomes of consecutive patients who had uneventful cataract surgery from April 2013 to September 2013 and used prednisolone acetate postoperatively were compared with the outcomes of consecutive patients who had uneventful cataract surgery from June 2014 to October 2014 and used difluprednate postoperatively.

Results: The study included 224 eyes treated with prednisolone acetate 4 times daily for 30 days and 225 eyes treated with difluprednate 2 times daily for 30 days. There was no significant difference between the 2 groups in age, sex, or race. In addition, the mean IOP did not differ significantly between the prednisolone acetate group and the difluprednate group at the preoperative measurement or 1 month after surgery, nor was there a difference in the 1-month change in IOP between groups. No association was found between the incidence of a 6 mm Hg or higher increase in IOP 1 month after surgery and steroid treatment. One month postoperatively, 4 eyes in the prednisolone acetate group and 5 eyes in the difluprednate group had an IOP higher than 21 mm Hg.

Conclusions: There was no significant difference in the mean IOP or percentages showing IOP elevation between eyes treated with difluprednate and eyes treated with prednisolone acetate after cataract surgery. This was likely the result of low-frequency dosing and short duration of steroid use.

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Over the past several decades, topical steroids such as prednisolone acetate 1.0% have been commonly used to treat postoperative inflammation after ophthalmic surgery. In June 2008, the U.S. Food and Drug Administration (FDA) approved a potent new steroid—difluprednate ophthalmic emulsion 0.05% (Durezol)—for the treatment of postoperative inflammation and pain. Difluprednate (difluoroprednisolone butyrate acetate) is a prednisolone derivative that was modified to increase its potency. The molecule was fluorinated at the C-6 and C-9 positions, and a butyrate ester was added to the C-17 position. The combination of these changes resulted in an increase in affinity for the glucocorticoid receptor. In addition, an acetate ester was added at position C-21 to enhance tissue penetration, which allows more of the active drug to reach the uvea. These modifications resulted in a drug with an active metabolite that is 56 times stronger than prednisolone.[1]

Smith et al.[2] found that difluprednate administered twice daily, when started 24 hours before cataract surgery, resulted in significantly decreased postoperative inflammation. Donnenfeld et al.[3] found that after cataract

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surgery, difluprednate in a high-dose pulsed-therapy regiment resulted in reduced inflammation and a more rapid return of vision than prednisolone acetate.

Because difluprednate has such high potency and steroids have known associations with intraocular pressure (IOP) elevation, there is concern that its use could result in glaucomatous optic neuropathy if elevated IOP is left untreated. Because of vigilant postoperative preventive measures, the reported incidence of this complication is low; however, approximately 8% of patients have a corticosteroid-induced IOP elevation after cataract surgery.[3]

In 2014, Jeng et al.[4] performed a retrospective chart review and concluded that eyes treated with difluprednate after vitreoretinal surgery were at an increased risk for developing a clinically significant increase in IOP than eyes treated with prednisolone acetate. We sought to determine whether there was a significantly greater incidence of corticosteroid-induced IOP response in eyes treated with difluprednate or eyes treated with prednisolone acetate for postoperative inflammation after cataract surgery.

PATIENTS AND METHODS

Study Cohort and Patient Enrollment

After the University of Michigan Institutional Review Board deemed this study to be not regulated, a retrospective medical record review of consecutive patients who had routine primary cataract extraction by 1 of 2 surgeons (E.P., P.E.) was performed.

Two cohorts were identified. The first cohort included patients who had cataract surgery from April 2013 through September 2013 and were treated postoperatively with prednisolone acetate 4 times a day for 30 days, nepafenac (Nevanac) 0.1% 3 times a day for 30 days, and ofloxacin 0.3% 4 times a day for 7 days. The second cohort included patients who had cataract surgery from June through October 2014 and were treated postoperatively with difluprednate 2 times a day for 30 days, nepafenac (Ilevro) 0.3% once a day for 30 days, and ofloxacin 0.3% 4 times a day for 7 days. Neither prednisolone acetate nor difluprednate was weaned over the 30-day administration period.

The data collected from the medical record review included age at the preoperative visit, sex, race, history of glaucoma, immunosuppression status, history of diabetes mellitus, preoperative IOP (the IOP measured at the preoperative cataract evaluation), IOP 1 day and 1 month postoperatively, and the type of tonometry used. To obtain IOP measurements, a Tono-Pen (Reichert Technologies), which is a handheld applanation tonometer, or a Goldmann applanation tonometer, which is a mounted tonometer, was used.

Consecutive patients aged 18 years or older, who had uneventful cataract surgery, were identified. The exclusion criteria included patients with a planned combined or complicated procedure (eg, hypermature cataract), patients who were comanaged by a referring optometrist who was outside of the TLC Eyecare and Laser Center provider network with incomplete data, and patients who had previous glaucoma surgeries including trabeculectomy or tube shunt placement.

Data from Jeng et al.[4] were used to estimate the sample size necessary to power this study adequately. Based on the premise that 20% of eyes treated with prednisolone acetate and 35% of eyes treated with difluprednate would develop an IOP spike, 151 eyes in each cohort would be required (using a 2-tailed test) to provide adequate error protection (Type 1 and II error probabilities of 0.05 and 0.20, respectively).

Main Outcome Measures

The measures used to determine the primary outcomes were the incidence of an increase in IOP higher than 6 mm Hg from the preoperative IOP (measured at the preoperative cataract evaluation) or an IOP higher than 21 mm Hg 1 month postoperatively.

Data Acquisition and Analysis

Characteristics of the sample were assessed with descriptive statistics, including means ± SD for continuous measures and frequencies and percentages for categorical measures, and stratified by steroid treatment group. Differences between the 2 treatment groups were assessed with 2-sample *t* tests and chi-square or Fisher exact tests for person-based measures. The IOP outcomes were compared between steroid treatment groups with linear mixed regression (for continuous IOP) and repeated measures logistic regression models (for threshold levels of IOP or IOP change). These models accounted for the correlation between the eyes of the same patient. The IOP thresholds were an increase in IOP higher than 6 mm Hg from baseline and an IOP higher than 21 mm Hg 1 month postoperatively. Statistical Analysis Software (version 9.4, SAS Institute, Inc.) was used for all statistical analyses.

RESULTS

The study assessed 243 patient records, including 123 patients (225 eyes) in the difluprednate cohort and 120 patients (224 eyes) in the prednisolone acetate cohort.

Table 1 shows the demographics by postoperative treatment group. There were no statistically significant differences between the 2 groups based on age (prednisolone acetate group 68.1 ± 11.4 years, range 33 to 86; difluprednate groups 67.1 ± 11.3 years, range 35 to 92) ($P = .4935$). There was also no statistically significant difference between the 2 groups in sex, race, diabetes status, glaucoma status, or systemic steroid/immunosuppressant use.

The preoperative IOP was similar between eyes treated postoperatively with difluprednate (15.4 ± 2.9 mm Hg) and eyes treated postoperatively with prednisolone acetate (14.8 ± 3.4 mm Hg) ($P = .0626$). One month postoperatively, there was no statistically significant difference in the mean IOP between the prednisolone acetate group (14.3 ± 3.4 mm Hg) and the difluprednate group (14.5 ± 3.6 mm Hg) ($P = .6582$). The change in IOP from baseline to 1 month postoperatively also was not significantly different between the 2 groups ($P = .2803$). Table 2 and Figure 1 show the IOP measurements between the groups. From baseline to 1 month postoperatively, 12 eyes (5.4%) in the prednisolone acetate group and 6 eyes (2.7%) in the difluprednate group had an IOP increase that was higher than 6 mm Hg ($P = .1975$), whereas 4 eyes (1.8%) in the prednisolone acetate group and 5 eyes (2.2%) in the difluprednate group had an IOP increase higher than 21 mm Hg ($P = .8209$).

Of the 6 eyes that were treated with difluprednate and had an IOP increase higher that 6 mm Hg from baseline, 1 eye had an IOP of 35 mm Hg 1 month postoperatively. One day postoperatively, this patient was treated with a short course of brimonidine but was no longer on topical glaucoma treatment 1 month postoperatively. The patient was ultimately diagnosed as a steroid responder. Another patient with a preexisting diagnosis of severe-stage primary open-angle glaucoma, who was using 4 topical glaucoma