Semi-fluorinated Alkane Eye Drops Reduce Signs and Symptoms of Evaporative Dry Eye Disease After Cataract Surgery

Hyeck-Soo Son, MD; Timur M. Yildirim, MD; Ramin Khoramnia, MD; Piyanut Poompokawat, MD; Michael C. Knorz, MD; Gerd U. Auffarth, MD, PhD

ABSTRACT

PURPOSE: To clinically evaluate the efficacy and tolerability of semi-fluorinated alkane eye drops (EvoTears; URSAPHARM GmbH) as ocular surface treatment after cataract surgery in patients with evaporative dry eye disease.

METHODS: This prospective, monocentric, open-label clinical trial included 40 patients undergoing cataract surgery and showing symptoms of evaporative dry eye disease as measured by the Symptom Assessment in Dry Eye (Visual Analogue Scale [VAS]) questionnaire, Ocular Surface Disease Index (OSDI), and tear break-up time (TBUT) of less than 10 seconds. EvoTears was prescribed four times a day for 5 weeks and administered 15 minutes after the standard postoperative topical anti-inflammatory regimen. The primary endpoint was the change in TBUT. Secondary endpoints included assessment of the subjective symptoms (VAS), corrected distance visual acuity (CDVA), slit-lamp examination, intraocular pressure, and Schirmer's test, which were evaluated at 1 day, 1 week, and 5 weeks postoperatively. At 5 weeks postoperatively, the tolerability and efficacy of EvoTears were evaluated by physicians and patients.

RESULTS: At 5 weeks postoperatively, the median TBUT increased from 6.8 (preoperative) to 14 seconds ($P < .001$) and the average total corneal staining score decreased from 3.53 (preoperative) to 2.36 ($P < .001$). The mean CDVA improved from 0.41 (preoperative) to 0.14 logMAR ($P < .001$) and there was a statistically significant decrease in all scores from the VAS questionnaire at 5 weeks postoperatively. There was no statistically significant change in Schirmer's test ($P = .150$).

CONCLUSIONS: EvoTears improved tear film, ocular surface, and subjective impressions of patients with dry eye disease 5 weeks after cataract surgery. Patients' and physicians' assessment indicated good efficacy and high tolerability of EvoTears, suggesting its suitability in postoperative management of the ocular surface in patients with dry eye disease.

[*J Refract Surg*. 2020;36(7):474-480.]

From David J. Apple International Laboratory for Ocular Pathology and International Vision Correction Research Centre, Department of Ophthalmology, University of Heidelberg, Heidelberg, Germany (HSS, TMY, RK, PP, GUA); and FreeVis LASIK Zentrum, Medical Faculty Mannheim, University of Heidelberg, Mannheim, Germany (MCK).

Submitted: November 27, 2019; Accepted: May 19, 2020

Supported by URSAPHARM GmbH, Saarbruecken, Germany. Clinical Trial Number (EUDAMED): CIV-16-12-017924.

Dr. Khoramnia has received grants from AcuFocus, Alcon Laboratories, Inc, Anew, Bausch & Lomb, Contamac, Johnson & Johnson, Kowa, Oculus Optikgeräte, PhysIOL, Presbia, Rayner, Santen, and SIFI, and has received financial support from Alcon Laboratories, Inc, Johnson & Johnson, and SIFI. Dr. Auffarth has received grants from AcuFocus, Alcon Laboratories, Inc, Alimera, Anew, Biotech, Carl Zeiss Meditec AG, Contamac, EyeYon, Glaukos, Hoya, Johnson & Johnson, Kowa, Oculentis/Teleon, Oculus Optikgeräte GmbH, PhysIOL, Rayner, Rheacell, Santan, SIFI, and URSAPHARM GmbH, and is a consultant for Johnson & Johnson. The remaining authors have no financial or proprietary interest in the materials presented herein.

Correspondence: Gerd U. Auffarth, MD, PhD, International Vision Correction Research Centre, Department of Ophthalmology, University of Heidelberg, INF 400, 69120 Heidelberg, Germany. Email: Gerd.Auffarth@med.uni-heidelberg.de

doi:10.3928/1081597X-20200519-01

Dry eye disease is a multifactorial dysfunction of the ocular surface characterized by altered structural integrity of the tear film.[1] Patients with dry eye disease present symptoms of ocular discomfort and report impairment in social functioning and reduced quality of life.[1-3] Generally, dry eye disease can be divided into "aqueous-deficient" and "evaporative" forms.[4] Although the former hyposecretory type is associated with Sjögren and non-Sjögren lacrimal diseases, the latter, more frequent, type is mainly caused by meibomian gland dysfunction.[1,4,5] The lipid coat of the tear film, primarily produced by the meibomian glands, covers the aqueous–mucous layers and plays a crucial role in ensuring tear stability and hindering evaporation by serving as a protective hydrophobic barrier.[6-8] An absent or insufficient lipid layer, as is the case in meibomian gland dysfunction, can precipitate up to a four-fold increase in tear evaporation.[8] Therefore, restoration of the lipid film and prevention of tear evaporation is the aim of effective therapy in evaporative dry eye disease.

Typically, dry eye disease is treated by topical substitution of the tear film.[9] However, most such "lubricants" are water based and contain viscous polymers such as hyaluronic acid, hydroxypropylmethyl-cellulose, or polyvidone to increase precorneal residence time.[9-11] Furthermore, they merely substitute the aqueous–mucous layers and often contain preservatives and additives that are associated with ocular toxicity.[11,12]

A novel lipophilic tear supplement, EvoTears (URSAPHARM GmbH), was introduced containing 100% perfluorohexyloctane, which is an aliphatic, semi-fluorinated hydrocarbon that is chemically, physically, and physiologically inert.[11] Due to its complete aqueous-free nature, it does not promote microbial growth or necessitate preservatives, demonstrates good spreading properties, and restores the lipid layer of the tear film, preventing excessive evaporation of the aqueous–mucous layers.[6,13,14] Clinical studies have shown significant beneficial effects of EvoTears in patients with evaporative dry eye disease[14] and meibomian gland dysfunction[13] when topically administered for 6 to 8 weeks.

In previous reports, the ocular surface of patients with dry eye disease has been shown to aggravate signs and symptoms after undergoing ocular interventions such as keratorefractive procedures or cataract surgeries.[15-19] Such postoperative aggravation of the ocular surface integrity is a problem that is often underestimated because it is not only associated with worsening of the dry eye symptoms that may further reduce the quality of life, but also with worse visual outcomes, instability of postoperative refraction, and side effects such as perception of halo and glare.

The aim of this prospective, single-center, open-labeled clinical trial was to evaluate the efficacy and tolerability of EvoTears as a postoperative ocular surface treatment after cataract surgery in patients with evaporative dry eye disease.

PATIENTS AND METHODS

Study Design

In this prospective, single-center, open-label clinical trial, 40 patients were enrolled and examined preoperatively and 1 day, 1 week, and 5 weeks postoperatively. Per patient, only one eye was included in the evaluation. The fellow eye was not scheduled for surgery during the time of the study, operated on during the time of the study but not assessed for changes in dry eye disease parameters in the course of the study, or already operated on before inclusion in the study. All patients were adequately informed and signed the informed consent form prior to study inclusion. The study complied with the German Act on Medical Devices, MPG§23b, and EN ISO 14155:2012-01 (Clinical Trial on Medical Devices for Use in Humans), was performed according to the guidelines of Good Clinical Practice, and adhered to the tenets of the Declaration of Helsinki and the laws of the Federal Republic of Germany. The trial protocol and patient information were approved by the local ethics committee. The registered clinical trial number (EUDAMED) is CIV-16-12-017924.

Inclusion criteria were adults with the presence of age-appropriate cataract for which standard cataract surgery was planned, preoperative subjective complaints indicating an evaporative dry eye disease for at least 3 months with a frequency and severity of complaints score of 2 of 10 or greater (Symptom Assessment in Dry Eye Visual Analog Scale [VAS] questionnaire) and Ocular Surface Disease Index (OSDI) score of 15 or greater, and fluorescein tear break-up time (TBUT) of 10 seconds or less. Exclusion criteria were dry eye due to systemic disease or concomitant medication or malign conditions, preoperative use of lipid-containing tear substitute for at least 3 months, simultaneous use of other therapeutic ophthalmics, ocular or systemic pathologies that may have an influence on the postoperative irritation (eg, acute viral or bacterial inflammation of the conjunctiva/cornea or chronic inflammatory/infectious uveitis), history of ocular surgery or punctum plugs during the past 3 months, malposition of the eyelids and/or lagophthalmos, contact lens wear up to 3 months before surgery, hypersensitivity against the ingredient (perfluorohexyloctane) of EvoTears, and concurrent pregnancy or lactation.

On inclusion in the study, all patients received EvoTears and were instructed to use them four times a

day, one drop in the conjunctival sac of the study eye in addition to the standard postoperative topical treatment (Isopto Max eye drops; Novartis Pharma GmbH) for 2 weeks and Isopto Max eye ointment (Novartis Pharma GmbH) 1x1/nocte for 1 week). No application of any eye drops was allowed up to 2 hours before an examination.

Preoperative and Postoperative Examination

At the preoperative visit, all patients were asked to fill out the VAS and OSDI questionnaires. The VAS questionnaire asked patients to judge their dry eye disease in terms of frequency of symptoms and severity of symptoms. Symptom assessment was evaluated by the VAS for the following symptoms: lacrimation, feeling of eye pressure, burning, foreign body sensation, mucus formation, and itching.[20] The preoperative scores are expressed on a VAS from 0 to 10. At 1 and 5 weeks postoperatively, subjective changes in these values were further evaluated via VAS and they were transformed into a decimal scale using the percentage change from baseline. The OSDI is another widely validated questionnaire for measuring the severity of dry eye disease and its categories are listed as: normal (0 to 12 points), mild (13 to 22 points), moderate (23 to 32 points), and severe (33 to 100 points).[20,21] In this study, the OSDI was used to verify the inclusion criteria of the patients preoperatively. It was not used postoperatively.

At all study visits, patients underwent an ophthalmological assessment including subjective refraction, corrected distance visual acuity (CDVA), slit-lamp examination, Goldmann applanation tonometry, and TBUT. Corneal staining was graded according to the Oxford grading scale.[22] At preoperative and 5-week postoperative visits, the Schirmer test was performed with paper strips inserted into the lower eyelid pouch for 5 minutes without anesthesia (Schirmer I).[13]

During the course of the trial, the physicians monitored any pathologic symptoms and adverse events. Patients who reported having problems were offered an immediate visit at the study site and examined by the physician.

Demographic Data

This study included 40 eyes of 40 patients with a mean age of 70.3 ± 9.4 years. There were 26 women (65%) and 14 men (35%). For the final data analysis, one patient was excluded from the postoperative data at the 5-week postoperative visit because this patient discontinued the use of EvoTears before the 5-week postoperative examination date due to subjective intolerance. At the preoperative visit, 38 patients (95%) had a "severe" OSDI total score, whereas 2 patients (5%) had a "moderate" OSDI total score. There were no patients with "normal" or "mild" preoperative OSDI scores.

Sample Size Calculation

For sample size calculation, previous literature was reviewed to define the approximate mean and standard deviation values for the primary endpoint, the TBUT.[14,23] The calculation was performed according to the methods of Dupont and Plummer.[24] Considering a power of 95% and an alpha value of 0.05, and under the hypothesis of preoperative and 5-week postoperative TBUT values of 6.5 and 9.0 seconds,[14,23] respectively, with a standard deviation of 4.0, a sample size of 35 patients was calculated. Considering a drop-out rate of 10% to 15%, 40 patients should have been enrolled in this study.

Statistical Analysis

Data analysis was performed using STATA 13.1 software (Stata Corp) and SPSS Statistics Software Package version 19.0 for Windows (SPSS, Inc). Normal distribution between preoperative and postoperative visits of the continuous variables was determined with the Kolmogorov-Smirnov test. The *t* test was used for parametric analysis. If a parametric analysis was not possible, the comparison of preoperative day 0 and postoperative day 35 after cataract surgery was done with the Wilcoxon signed-rank test. Paired categorical data were evaluated with the exact McNemar test in table 2 × 2.

Continuous data were presented as mean and standard deviation or median and range, whereas categorical data were expressed as percentages and absolute values.

For all statistical tests, a *P* value of less than .05 was considered statistically significant.

RESULTS

Table 1 shows the mean values of the TBUT, CDVA, Schirmer test, corneal staining score, and intraocular pressure at given visit dates.

TBUT

At 5 weeks postoperatively, there was a statistically significant increase ($P < .001$) in the mean TBUT value (13.5 ± 6.7 seconds) compared to the preoperative visit (6.5 ± 1.6 seconds) (**Figure A**, available in the online version of this article).

CDVA

At 5 weeks postoperatively, the mean CDVA value (0.14 ± 0.24 logMAR) improved statistically significantly ($P < .001$) compared to the preoperative visit (0.41 ± 0.26 logMAR).

TABLE 1

Mean TBUT, CDVA, Schirmer Test, Corneal Staining, and IOP Values[a]

Parameter	Preoperative (n = 40)	1 Day Postoperative (n = 40)	1 Week Postoperative (n = 40)	5 Weeks Postoperative (n = 39)	*P*[b]
TBUT (seconds)	6.5 ± 1.6	7.9 ± 2.4	9.8 ± 3.4	13.5 ± 6.7	< .001[c]
CDVA (logMAR)	0.41 ± 0.26	0.36 ± 0.29	0.17 ± 0.28	0.14 ± 0.24	< .001[c]
Schirmer test (mm/5 min)	18.18 ± 8.32	–	–	15.77 ± 9.47	.15
Corneal staining	3.53 ± 2.00	4.80 ± 2.23	4.38 ± 2.64	2.36 ± 2.03	< .004[c]
IOP (mm Hg)	14.4 ± 2.7	14.4 ± 3.5	14.2 ± 2.6	14.3 ± 4.2	.3815

IOP = intraocular pressure; TBUT = tear break-up time; CDVA = corrected distance visual acuity
[a]*Values are presented as mean ± standard deviation.*
[b]*P values refer to the difference in measured mean values between preoperative and 5 weeks postoperative visits.*
[c]*Statistical significance (P < .05).*

TABLE 2

Symptom Assessment in Dry Eye Questionnaire Scores Expressed on a Visual Analog Scale[a]

Parameter	Preoperative (n = 40)	1 Week Postoperative (n = 40)	5 Weeks Postoperative (n = 39)	*P*[b]
Frequency of symptoms	5.5 ± 2.3	4.1 ± 3.2	2.5 ± 2.6	< .001[c]
Severity of symptoms	5.4 ± 2.1	4.5 ± 3.7	2.2 ± 2.3	< .001[c]
Lacrimation	4.2 ± 2.6	3.3 ± 3.3	2.8 ± 4.0	< .001[c]
Feeling of eye pressure	2.4 ± 2.3	1.8 ± 2.4	1.1 ± 1.5	< .001[c]
Burning sensation	3.6 ± 2.4	2.8 ± 2.5	1.5 ± 1.8	< .001[c]
Foreign body sensation	4.4 ± 2.9	4.0 ± 3.8	2.6 ± 3.5	< .002[c]
Mucus formation	1.7 ± 2.3	1.3 ± .0	1.0 ± 2.0	< .0016[c]
Itching	3.4 ± 2.5	2.0 ± 1.9	1.2 ± 1.6	< .001[c]

[a]*Values are presented as mean ± standard deviation.*
[b]*P values refer to the difference in measured mean values between preoperative and 5 weeks postoperative visits.*
[c]*Statistical significance (P < .05).*

SCHIRMER TEST

Between the preoperative and 5-week postoperative visits, there was no statistically significant difference in the mean Schirmer test values ($P = .150$) (**Figure A**).

CORNEAL STAINING SCORE

The mean total corneal staining score at the 5-week postoperative visit (2.36 ± 2.03) showed statistically significant improvement ($P < .004$) compared to the preoperative visit (3.53 ± 2.00) (**Figure A**).

INTRAOCULAR PRESSURE

The intraocular pressure did not show any statistically significant change during the trial ($P = .3815$).

VAS QUESTIONNAIRE

Table 2 shows the scores given by the patients at preoperative and 1 and 5 weeks postoperative visits. With respect to the baseline values at the preoperative visit, all parameters improved statistically significantly at the 5-week postoperative visit (**Figure B**, available in the online version of this article).

SUBJECTIVE ASSESSMENT OF TOLERABILITY AND EFFECTIVENESS

Table 3 demonstrates the patient's and physician's assessment of efficacy and tolerability at the 5-week postoperative visit. The tolerability of EvoTears was rated as "impeccable" in 97.4% of patients and physicians, whereas its efficacy was evaluated as "impeccable" or "acceptable" by 89.7% of physicians.

ADVERSE EVENTS

A total of 12 adverse events was reported in 8 patients (**Table A**, available in the online version of this article). Seven adverse events were assessed as being related to the cataract surgery. Two adverse events (one case of skin irritation and one of conjunctival redness) were classified as "not assessable retrospectively" and three adverse events (subjective incompatibil-

TABLE 3

Patient and Physician Assessment of Tolerability and Efficacy at 5-Week Postoperative Visit

Parameter	Patient Tolerability	Physician Tolerability	Physician Efficacy
Impeccable	38 (97.4%)	38 (97.4%)	25 (64.1%)
Acceptable	0 (0.0%)	1 (2.6%)	10 (25.6%)
Not acceptable	1 (2.6%)	0 (0.0%)	4 (10.3%)
Subtotal	39	39	39

ity with postoperative eye medication, skin rash, and blepharitis) were classified as "EvoTears suspected of causing adverse event." None of those was classified as a serious adverse device effect (incident according to applicable legislation).

DISCUSSION

Surgical interventions such as cataract surgery have been shown to cause damage to the sensory nerves of the cornea, hindering proper neural feedback and leading to a reduced blinking rate and decreased tear secretion.[17,25-29] Consequently, patients who already suffer from dry eye disease may show aggravated ocular surface postoperatively.[17,28,30] Furthermore, Ishrat et al[17] assessed the incidence of dry eye symptoms after cataract surgery in patients who did not show any clinical signs of dry eye disease preoperatively and reported that 42% of patients showed signs of mild to severe dry eye at 1 week postoperatively, suggesting that patients without dry eye disease may also be at risk of developing dry eye symptoms after cataract surgery.

Postoperative dry eye may be induced by a confluence of multiple factors. Phototoxic effects from the light exposure of the operating microscope,[27,31,32] elevated levels of inflammatory cytokines in lacrimal tears,[33] and the administration of topical anesthesia and a postoperative antibiotic regimen containing preservatives[29] are among the factors that may have a negative impact on the stability of the tear film.

Previous studies reported that the meibomian glands may also be affected after cataract surgery.[28,34] Park et al[34] observed a statistically significant worsening of the meibomian gland parameters including eyelid margin abnormality, meibum expressibility, and meibum quality in patients with dry eye at up to 2 months after cataract surgery. The results were statistically significantly worse than those measured in the group without dry eye. The authors hypothesized that such functional and structural changes of the meibomian glands may have been caused by the postoperative ocular surface inflammation, eyelid dysfunction due to intraoperative placement of an eyelid speculum, and decrease in blink rate triggered by reduced corneal sensation.[34] In another study, Kim et al[26] assessed the thickness of the tear film lipid layer after cataract surgery to evaluate the impact of surgery on dry eye surface and reported statistically significant thinning of the lipid layer at 1 month postoperatively. Furthermore, the authors observed significantly shorter TBUT, higher OSDI scores, and worse meibum scores,[28] reaffirming the importance of the lipid layer in preserving the integrity of the ocular surface.

EvoTears eye drops consist of 100% perfluorohexyloctane. This aliphatic, partly fluorinated hydrocarbon is a chemically and physically inert substance that stabilizes the lipid phase of the tear film.[35,36] Numerous studies have evaluated and reported the beneficial effects of EvoTears in patients with dry eye disease.[6,11,13,14] In a prospective observational study, Steven et al[14] administered EvoTears four times a day for 6 weeks in patients with evaporative dry eye disease and observed significant improvements of the tear film stability, TBUT, and Schirmer I, and a significant reduction of overall corneal staining. In another study, Steven et al[13] assessed the effect of perfluorohexyloctane in patients with meibomian gland dysfunction and reported that 6 to 8 weeks of topical application not only led to increased meibum quality, quantity, and expressibility, but also improved TBUT and corneal staining.

Meibomian gland dysfunction is considered the main cause of evaporative dry eye disease[1,4,5] and thus restoration of the tear film lipid layer is essential for its treatment. This study evaluated the efficacy of lipophilic, aqueous-free EvoTears as postoperative ocular surface treatment in patients with evaporative dry eye disease undergoing cataract surgery. The results observed in this study were similar to those in the aforementioned studies. The application of EvoTears four times a day for 5 weeks along with the standard postoperative anti-inflammatory regimen led to marked improvement of dry eye disease parameters, particularly TBUT, the mean value of which almost doubled at 5 weeks postoperatively compared to the preoperative value. Moreover, there was a statistically significant reduction of total corneal staining score and statistically significant decrease in all scores of the VAS questionnaire at 5 weeks

postoperatively. The Schirmer test showed a slight decrease compared to its preoperative value, yet the difference was not statistically significant.

The positive results observed in this study were also in accordance with the subjective assessment of the patients and physicians. All except one patient rated the tolerability of EvoTears as "impeccable," whereas all physicians rated its tolerability as either "impeccable" or "acceptable." Furthermore, 89.7% of physicians rated the efficacy of EvoTears as "impeccable" or "acceptable."

Overall, this study demonstrated a good safety profile. Of those three adverse events that were suspected to be related to EvoTears, two were considered as minor (skin rash on the eyelid and blepharitis), whereas the third, although also considered minor (incompatibility with postoperative eye medication), led to discontinuation of the treatment due to subjective incompatibility.

The beneficial effect of EvoTears observed in this study may be ascribable to an array of properties compared to the other commercially available artificial tear supplements, of which most are water based. First, perfluorohexyloctane has been shown to possess good spreading abilities[37] due to low interfacial tension and thereby reduce friction of the eyelids on the ocular surface with each eye blink.[38,39] Because inflammation plays a central role in dry eye disease, less mechanical force on corneal and conjunctival epithelium may help soothe the ocular surface. Furthermore, thanks to its compelling spreading property, a significantly smaller droplet is sufficient to cover the ocular surface,[14] which in turn minimizes the blurring effect on vision after each instillation.[9] Because the drop size of 10 µL corresponds to the volume of the conjunctival sac, there is no rinsing of the eye after application of EvoTears. Second, perfluorohexyloctane is amphiphilic and able to dissolve lipids, which may contribute to dissolution of thickened meibum that could be blocking the meibomian glands,[38,39] resulting in lipid layer stabilization of the tear film. Finally, thanks to its water-free nature, it discourages microbial growth and does not require any preservatives,[6,13] allowing patients to administer drops more frequently without having to worry about the potential toxic effects of preservatives.[11,12]

This study is limited to the extent that it is a prospective open-label study without a control group, which makes it difficult to assess the potential placebo effects. Another limitation is that the steroids applied after cataract surgery may also lead to an improvement in dry eye symptoms and clinical parameters.[40] However, this positive effect on dry eye disease parameters may also be "offset" by the ocular surface toxicity caused by the benzalkonium chloride, which is also contained in our standard postoperative topical anti-inflammatory regimen and has been shown to induce tear film instability and dry eye sensation.[41,42] Furthermore, fluctuations in subjective assessments due to environmental and seasonal factors cannot be excluded. Longer follow-up periods may also be necessary to determine the long-term benefits of EvoTears in patients with evaporative dry eye disease after ocular surgery. Yet, because an eye is considered to be "recovered from cataract surgery" approximately 5 weeks postoperatively, it is regarded as a "normal" dry eye thereafter. Thus, the long-term observation also corresponds to its clinical efficacy in "normal" patients with dry eye disease.

Our results showed that EvoTears is effective in treating patients with evaporative dry eye disease undergoing cataract surgery, as shown by significant improvements in TBUT, corneal staining, and subjective assessment of dry eye symptoms. Furthermore, both the patients' and physicians' assessment indicated high tolerability and a reliable safety profile, suggesting its suitability in postoperative management of the ocular surface in patients with dry eye disease.

AUTHOR CONTRIBUTIONS

Study concept and design (GUA); data collection (HSS, TMY, RK, PP, GUA); analysis and interpretation of data (HSS, TMY, RK, PP, MCK, GUA); writing the manuscript (HSS, TMY, PP); critical revision of the manuscript (RK, MCK, GUA); statistical expertise (HSS); administrative, technical, or material support (GUA); supervision (RK, GUA)

REFERENCES

1. Nelson JD, Craig JP, Akpek EK, et al. TFOS DEWS II Introduction. *Ocul Surf*. 2017;15(3):269-275. doi:10.1016/j.jtos.2017.05.005
2. Uchino M, Schaumberg DA. Dry eye disease: impact on quality of life and vision. *Curr Ophthalmol Rep*. 2013;1(2):51-57. doi:10.1007/s40135-013-0009-1
3. Dana R, Bradley JL, Guerin A, et al. Estimated prevalence and incidence of dry eye disease based on coding analysis of a large, all-age United States Health Care System. *Am J Ophthalmol*. 2019;202:47-54. doi:10.1016/j.ajo.2019.01.026
4. Lemp MA. The definition and classification of dry eye disease: report of the Definition and Classification Subcommittee of the International Dry Eye WorkShop (2007). *Ocul Surf*. 2007;5(2):75-92. doi:10.1016/S1542-0124(12)70081-2
5. Heiligenhaus A, Koch JM, Kruse FE, Schwarz C, Waubke TN. Diagnosis and differentiation of dry eye disorders [article in German]. *Ophthalmologe*. 1995;92(1):6-11.
6. Agarwal P, Khun D, Krösser S, et al. Preclinical studies evaluating the effect of semifluorinated alkanes on ocular surface and tear fluid dynamics. *Ocul Surf*. 2019;17(2):241-249. doi:10.1016/j.jtos.2019.02.010
7. Bron AJ, Tiffany JM, Gouveia SM, Yokoi N, Voon LW. Functional aspects of the tear film lipid layer. *Exp Eye Res*. 2004;78(3):347-360. doi:10.1016/j.exer.2003.09.019

8. Craig JP, Tomlinson A. Importance of the lipid layer in human tear film stability and evaporation. *Optom Vis Sci*. 1997;74(1):8-13. doi:10.1097/00006324-199701000-00014

9. Jones L, Downie LE, Korb D, et al. TFOS DEWS II Management and Therapy Report. *Ocul Surf*. 2017;15(3):575-628. doi:10.1016/j.jtos.2017.05.006

10. Meseguer G, Buri P, Plazonnet B, Rozier A, Gurny R. Gamma scintigraphic comparison of eyedrops containing pilocarpine in healthy volunteers. *J Ocul Pharmacol Ther*. 1996;12(4):481-488. doi:10.1089/jop.1996.12.481

11. Agarwal P, Scherer D, Günther B, Rupenthal ID. Semifluorinated alkane based systems for enhanced corneal penetration of poorly soluble drugs. *Int J Pharm*. 2018;538(1-2):119-129. doi:10.1016/j.ijpharm.2018.01.019

12. Yang W, Acosta D. Cytotoxicity potential of surfactant mixtures evaluated by primary cultures of rabbit corneal epithelial cells. *Toxicol Lett*. 1994;70(3):309-318. doi:10.1016/0378-4274(94)90125-2

13. Steven P, Augustin AJ, Geerling G, et al. Semifluorinated alkane eye drops for treatment of dry eye disease due to meibomian gland disease. *J Ocul Pharmacol Ther*. 2017;33(9):678-685. doi:10.1089/jop.2017.0042

14. Steven P, Scherer D, Krösser S, Beckert M, Cursiefen C, Kaercher T. Semifluorinated alkane eye drops for treatment of dry eye disease—a prospective, multicenter noninterventional study. *J Ocul Pharmacol Ther*. 2015;31(8):498-503. doi:10.1089/jop.2015.0048

15. Gomes JAP, Azar DT, Baudouin C, et al. TFOS DEWS II iatrogenic report. *Ocul Surf*. 2017;15(3):511-538. doi:10.1016/j.jtos.2017.05.004

16. Shao D, Zhu X, Sun W, Cheng P, Chen W, Wang H. Effects of femtosecond laser-assisted cataract surgery on dry eye. *Exp Ther Med*. 2018;16(6):5073-5078. doi:10.3892/etm.2018.6862

17. Ishrat S, Nema N, Chandravanshi SCL. Incidence and pattern of dry eye after cataract surgery. *Saudi J Ophthalmol*. 2019;33(1):34-40. doi:10.1016/j.sjopt.2018.10.009

18. Gupta PK, Drinkwater OJ, VanDusen KW, Brissette AR, Starr CE. Prevalence of ocular surface dysfunction in patients presenting for cataract surgery evaluation. *J Cataract Refract Surg*. 2018;44(9):1090-1096. doi:10.1016/j.jcrs.2018.06.026

19. Miyake K, Yokoi N. Influence on ocular surface after cataract surgery and effect of topical diquafosol on postoperative dry eye: a multicenter prospective randomized study. *Clin Ophthalmol*. 2017;11:529-540. doi:10.2147/OPTH.S129178

20. Amparo F, Schaumberg DA, Dana R. Comparison of two questionnaires for dry eye symptom assessment: the Ocular Surface Disease Index and the Symptom Assessment in Dry Eye. *Ophthalmology*. 2015;122(7):1498-1503. doi:10.1016/j.ophtha.2015.02.037

21. Schiffman RM, Christianson MD, Jacobsen G, Hirsch JD, Reis BL. Reliability and validity of the Ocular Surface Disease Index. *Arch Ophthalmol*. 2000;118(5):615-621. doi:10.1001/archopht.118.5.615

22. Bron AJ, Evans VE, Smith JA. Grading of corneal and conjunctival staining in the context of other dry eye tests. *Cornea*. 2003;22(7):640-650. doi:10.1097/00003226-200310000-00008

23. Mencucci R, Boccalini C, Caputo R, Favuzza E. Effect of a hyaluronic acid and carboxymethylcellulose ophthalmic solution on ocular comfort and tear-film instability after cataract surgery. *J Cataract Refract Surg*. 2015;41(8):1699-1704. doi:10.1016/j.jcrs.2014.12.056

24. Dupont WD, Plummer WD Jr. Power and sample size calculations: a review and computer program. *Control Clin Trials*. 1990;11(2):116-128. doi:10.1016/0197-2456(90)90005-M

25. Sacchi M, de Cilla S, Carini E, et al. Corneal changes after cataract surgery: short term results of an in vivo confocal microscopy study. *Invest Ophthalmol Vis Sci*. 2009;50(13):6095.

26. Kim JS, Lee H, Choi S, Kim EK, Seo KY, Kim TI. Assessment of the tear film lipid layer thickness after cataract surgery. *Semin Ophthalmol*. 2018;33(2):231-236.

27. Cho YK, Kim MS. Dry eye after cataract surgery and associated intraoperative risk factors. *Korean J Ophthalmol*. 2009;23(2):65-73. doi:10.3341/kjo.2009.23.2.65

28. Cetinkaya S, Mestan E, Acir NO, Cetinkaya YF, Dadaci Z, Yener HI. The course of dry eye after phacoemulsification surgery. *BMC Ophthalmol*. 2015;15(1):68. doi:10.1186/s12886-015-0058-3

29. Kasetsuwan N, Satitpitakul V, Changul T, Jariyakosol S. Incidence and pattern of dry eye after cataract surgery. *PLoS One*. 2013;8(11):e78657. doi:10.1371/journal.pone.0078657

30. Roberts CW, Elie ER. Dry eye symptoms following cataract surgery. *Insight*. 2007;32(1):14-21.

31. Hwang HB, Kim HS. Phototoxic effects of an operating microscope on the ocular surface and tear film. *Cornea*. 2014;33(1):82-90. doi:10.1097/ICO.0000000000000001

32. Oh T, Jung Y, Chang D, Kim J, Kim H. Changes in the tear film and ocular surface after cataract surgery. *Jpn J Ophthalmol*. 2012;56(2):113-118. doi:10.1007/s10384-012-0117-8

33. Acera A, Rocha G, Vecino E, Lema I, Durán JA. Inflammatory markers in the tears of patients with ocular surface disease. *Ophthalmic Res*. 2008;40(6):315-321. doi:10.1159/000150445

34. Park Y, Hwang HB, Kim HS. Observation of influence of cataract surgery on the ocular surface. *PLoS One*. 2016;11(10):e0152460. doi:10.1371/journal.pone.0152460

35. Joussen AM, Rizzo S, Kirchhof B, et al; HSO-Study Group. Heavy silicone oil versus standard silicone oil in as vitreous tamponade in inferior PVR (HSO Study): interim analysis. *Acta Ophthalmol*. 2011;89(6):e483-e489. doi:10.1111/j.1755-3768.2011.02139.x

36. Meinert H, Roy T. Semifluorinated alkanes: a new class of compounds with outstanding properties for use in ophthalmology. *Eur J Ophthalmol*. 2000;10(3):189-197. doi:10.1177/112067210001000301

37. Kim YK, Gunther B, Meinert H. A new, heavier-than-water silicone oil: a solution of perfluorohexyloctane in polydimethylsiloxane. *Eur J Ophthalmol*. 2005;15(5):627-637. doi:10.1177/112067210501500514

38. Broniatowski M, Dynarowicz-Latka P. Semifluorinated alkanes—primitive surfactants of fascinating properties. *Adv Colloid Interface Sci*. 2008;138(2):63-83. doi:10.1016/j.cis.2007.11.002

39. Obraztsov VV, Neslund GG, Kornbrust ES, Flaim SF, Woods CM. In vitro cellular effects of perfluorochemicals correlate with their lipid solubility. *Am J Physiol Lung Cell Mol Physiol*. 2000;278(5):L1018-L1024. doi:10.1152/ajplung.2000.278.5.L1018

40. Pinto-Fraga J, López-Miguel A, González-García MJ, et al. Topical fluorometholone protects the ocular surface of dry eye patients from desiccating stress: a randomized controlled clinical trial. *Ophthalmology*. 2016;123(1):141-153. doi:10.1016/j.ophtha.2015.09.029

41. Fraunfelder FT, Sciubba JJ, Mathers WD. The role of medications in causing dry eye. *J Ophthalmol*. 2012;2012:285851. doi:10.1155/2012/285851

42. Baudouin C, Labbé A, Liang H, Pauly A, Brignole-Baudouin F. Preservatives in eyedrops: the good, the bad and the ugly. *Prog Retin Eye Res*. 2010;29(4):312-334. doi:10.1016/j.preteyeres.2010.03.001

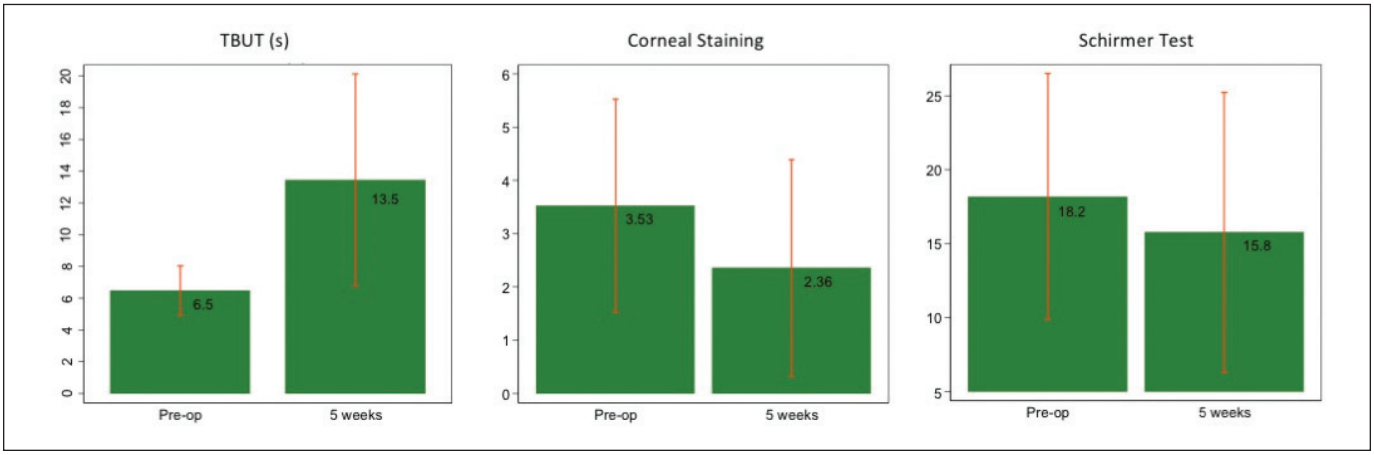

Figure A. Mean values of tear break-up time (TBUT), corneal staining, and Schirmer test measured preoperatively and at 5 weeks postoperatively.

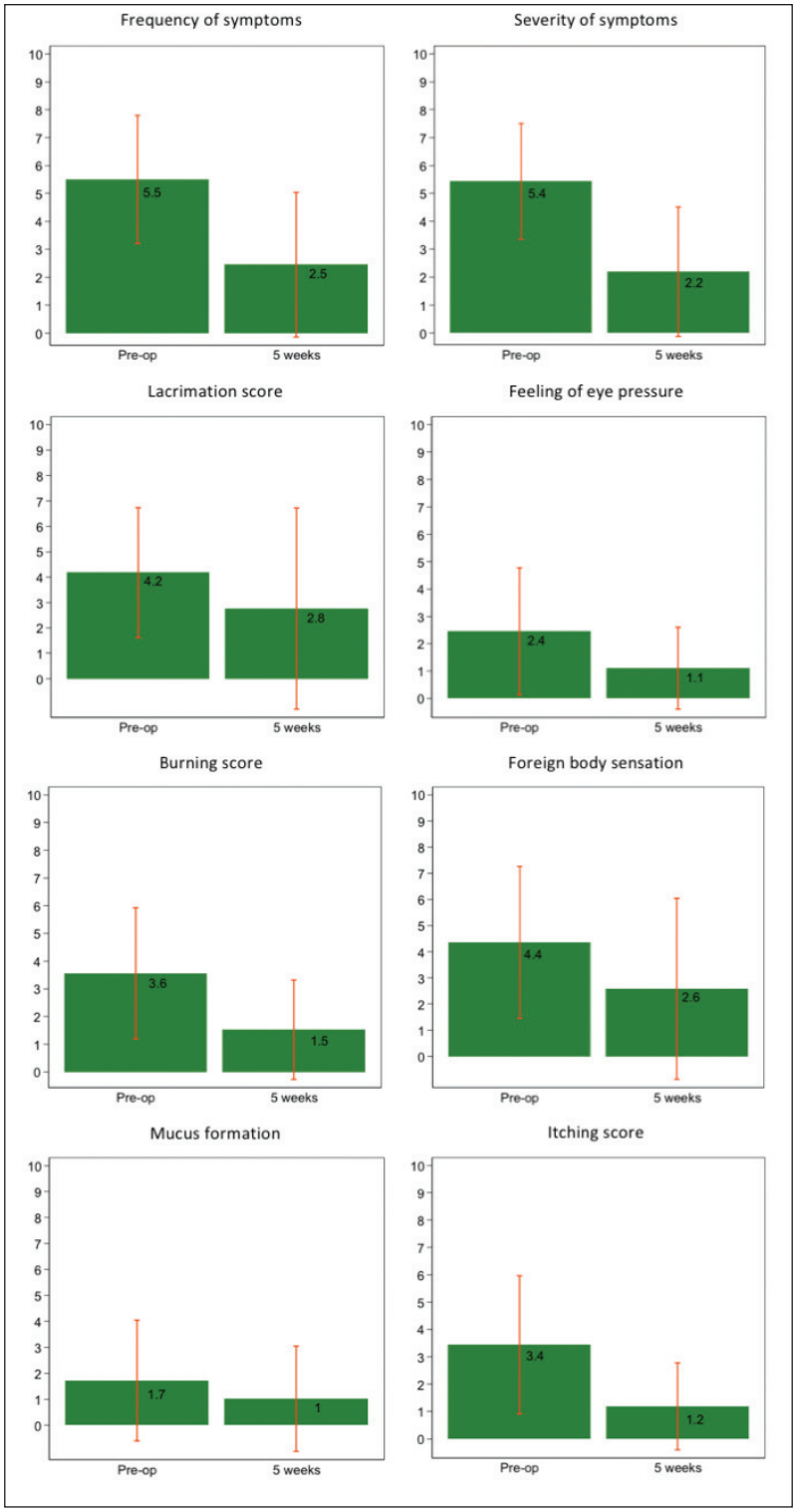

Figure B. Visual Analogue Scale questionnaire results as expressed on a visual analog scale at preoperative and 5 weeks postoperative visits.

TABLE A

Adverse Events

Patient No.	Event	Severity	Drops Suspected of Causing Adverse Event	Treatment Continued?
1	Skin irritation	Minor	Not assessable retrospectively	Yes
2	Conjunctival redness	Minor	Not assessable retrospectively	Yes
2	Damaged teeth during anesthesia induction	Severe	No	Yes
3	Vitreous prolapse	Severe	No	Yes
4	Open posterior capsule	Minor	No	Yes
4	Postoperative corneal edema	Minor	No	Yes
5	Intraocular pressure increase	Minor	No	Yes
5	Corneal erosion minor	No	Yes	
5	Intraocular pressure increase	Minor	No	Yes
6	Incompatibility with postoperative eye medication	Minor	Yes	No
7	Skin rash (on the eyelid)	Minor	Yes	Yes
8	Blepharitis	Minor	Yes	Yes