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ORIGINAL RESEARCH

Impact of Perioperative Dry Eye Treatment with Rebamipide Versus Artificial Tears on Visual Outcomes After Cataract Surgery in Japanese Population

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ABSTRACT

Introduction: The present study aimed to compare the effects of rebamipide and artificial tears during the perioperative period of cataract surgery on the postoperative visual outcomes.
Methods: Seventy-two eyes from 36 patients with a cataract were enrolled. Rebamipide (group R) was administered in one eye and Mytear® artificial tear ophthalmic solution (group A) in the other eye from 4 weeks preoperatively to 3 months postoperatively. Tear breakup time (TBUT), high-order aberrations (HOAs), superficial punctate keratopathy in the central part of the cornea (C-SPK), and corrected distance visual acuity (CDVA) were assessed at baseline, 1 week, 1 month, and 3 months after cataract surgery with trifocal intraocular lens (IOL) implantation. Contrast sensitivity and disability glare with visual angle values compatible with spatial frequencies of 1.1, 1.8, 2.9, 4.5, 7.1, and 10.2 cycles/degree (CPD) were evaluated postoperatively. Between-group differences of all variables were analyzed.
Results: At baseline, no significant differences in the variables were noted between the two groups. Mean TBUT was significantly higher, while mean C-SPK and HOAs were significantly lower in group R than in group A at each assessment. Mean CDVA was significantly higher at 1 week and 1 month postoperatively in group R compared with group A; this value was not significant at 3 months. Between-group differences in contrast sensitivity and disability glare were statistically significant at all spatial frequencies, 1 week and 1 month postoperatively. At 3 months postoperatively, there were significant differences in contrast sensitivity and disability glare at most spatial frequencies.
Conclusion: Dry eye management with rebamipide in the perioperative period of cataract surgery with trifocal IOL implantation was significantly more effective than artificial tears in improving ocular surface condition, contrast sensitivity, and disability glare postoperatively.

Keywords: Artificial tears; Cataract surgery; Contrast sensitivity; Cyclosporine; Disability glare; Multifocal; Ocular; Rebamipide

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Key Summary Points

Why carry out this study?

Patients with dry eyes are susceptible to a decrease in postoperative visual quality after cataract surgery with trifocal intraocular lens implantation.

The superiority of rebamipide over artificial tears has been previously demonstrated, but its effect during the perioperative period of cataract surgery on the postoperative visual outcomes is undetermined.

Herein, we examined the effects of perioperative administration of rebamipide and artificial tears on postoperative ocular surface condition and quality of vision.

What was learned from the study?

Dry eye treatment with rebamipide during the perioperative period of cataract surgery yielded better results compared to artificial tears in improving postoperative tear film stability and corneal surface condition.

In addition, rebamipide was significantly more effective than artificial tears in improving ocular surface condition, visual acuity, contrast sensitivity, and disability glare postoperatively.

INTRODUCTION

Multifocal intraocular lenses (IOLs) have gained popularity in the field of cataract surgery owing to patients' increasing demand for independence from spectacles [1]. In particular, trifocal IOLs, which distribute light into three focal points, have interested specialists in recent years [1]. However, the simultaneous focusing of three points results in an inherent loss of contrast sensitivity, which causes degradation of the quality of vision [2]. Additionally, dry eye can also worsen contrast sensitivity and disability glare (the decrease of contrast sensitivity caused by glare) [3, 4]. Consequently, the combination of multifocal IOLs and dry eye condition can lead to reduced quality of vision [4]. It was reported that approximately 60% of patients planning to undergo a cataract operation demonstrate short tear breakup time (TBUT), and about 35% show corneal staining in the central part of the cornea [5]. It has also been found that a cataract operation can cause dry eye as well as exacerbate existing dry eye [6, 7]. These findings indicate that patients with a cataract and dry eyes are more vulnerable to a decrease in the quality of vision postoperatively, especially those receiving multifocal IOLs.

Rebamipide (Otsuka Pharmaceutical Co, Ltd, Tokyo, Japan), which is a quinolinone derivative with mucin secretagogue activity, has the ability to improve tear film stability and ocular surface condition by increasing mucin-like substances and reducing inflammatory cytokines [8]. It was observed that rebamipide produced a mucin-like glycoprotein and expressed MUC1 and MUC4 when human corneal epithelial cells were cultured with rebamipide [9]. Furthermore, we have demonstrated previously that dry eye treatment with rebamipide before preoperative examination improved the refractive accuracy of cataract surgery [10]. In light of these findings, we predicted that dry eye treatment with rebamipide in the perioperative period of a cataract operation may improve the ocular surface condition and quality of vision postoperatively.

Studies in the past have demonstrated the positive effect of artificial tears on corneal surface irregularity [11], as well as the superiority of rebamipide over artificial tears in improving ocular surface condition [12]. However, no study has yet investigated the effect of rebamipide administration during the perioperative period of cataract surgery on the postoperative visual outcomes. Therefore, the aim of the present study was to compare the effects of rebamipide and artificial tears during the perioperative period of cataract surgery on

postoperative ocular surface condition and quality of vision.

METHODS

This single-center, prospective, open-label study included 72 eyes from 36 patients. All patients were scheduled to undergo bilateral cataract surgery with diffractive trifocal IOL implantation (AcrySof IQ PanOptix, Alcon Laboratories, Fort Worth, TX, USA) and were diagnosed with dry eye. This study received ethical approval from the committees of Yokosuka Chuo Eye Clinic and Tsurumi Chuo Eye Clinic (reference number 2021-003). The study was performed in accordance with the Helsinki Declaration of 1964, and its later amendments. Before starting the research process, detailed information was provided, and written informed consent was obtained from all subjects to participate in this study and publish the resulting data.

Patients

Patients between 67 and 79 years of age who were diagnosed with dry eye on the basis of the Japanese dry eye diagnostic criteria (TBUT $\leq$ 5 s and dry eye symptoms like eye discomfort and visual disturbance) [13] were eligible for this study. The subjective symptoms were assessed with the Japanese version of the Ocular Surface Disease Index (J-OSDI) [14]. On the basis of the results of preoperative examinations, it was speculated that the patients were most likely to improve their vision to 0.2 (logMAR) or more postoperatively. Baseline dry eye examinations for all patients were performed on the day of prescribing rebamipide or artificial tears, before the first administration of the eye drops. Patients who had previously used rebamipide, artificial tears, contact lenses, or those with a medical history of intraocular surgery, ocular trauma, ocular inflammation, ocular scarring, ocular dystrophy, and any condition causing ocular surface irregularity were excluded from the study.

Dry Eye Treatment

A single doctor was assigned the responsibility for prescribing eye drops for the dry eye. Either 2% rebamipide ophthalmic suspension (Mucosta Ophthalmic Suspension UD2%; Otsuka Pharmaceutical Co) (group R) or artificial tears (Mytear® ophthalmic solution; Senju Pharmaceutical Co, Ltd, Osaka, Japan) (group A) was prescribed for the first eye operation and vice versa for the second eye operation, simultaneously. Mytear contains sodium chloride (5.5 mg), potassium chloride (1.6 mg), dried sodium carbonate (0.6 mg), dibasic sodium phosphate hydrate (1.8 mg), and boric acid (12 mg) in a 1 mL solution and has a viscosity of 2.22 mm^2/s (at 20 °C $\pm$ 0.1 °C). Patients ceased using all other eye drops before initiating dry eye treatment and used rebamipide or the prescribed artificial tears from 4 weeks to 3 months after surgery. The treatment onset and duration were chosen according to a similar previous study which investigated the effect of rebamipide administration during the perioperative period of cataract surgery [12].

Routine Pre- and Postoperative Eye Drops

All patients were instructed to use moxifloxacin eye drops (Vigamox®; Alcon Laboratories, Inc, Fort Worth, TX, USA) four times a day and 0.1% nepafenac ophthalmic suspension (Nevanac®; Alcon Laboratories, Inc, Fort Worth, TX, USA) three times a day for 3 days before the operation. Following the operation, they were instructed to use moxifloxacin four times a day and 0.1% betamethasone sodium phosphate eye drops (Rinderon, Shionogi Pharmaceutical, Osaka, Japan) four times a day for 2 weeks and bromfenac ophthalmic solution 0.09% (Xibrom™, ISTA Pharmaceuticals Inc, Irvine, CA, USA) twice a day for 1 month.

Surgical Technique

All operations were performed at the same facility by one surgeon. Femtosecond laser-assisted cataract surgery (FLACS) with implantation of a one-piece trifocal diffractive IOL

(PanOptix, Alcon Laboratories, Fort Worth, TX, USA) was scheduled for all cases. As planned, FLACS was performed using the femtosecond laser (LenSx, Alcon Laboratories, Fort Worth, TX, USA), and 5.0-mm capsulotomy centered on White-to-White was created with 8.0 mJ of energy (spot and layer separations 9 μm each). Nuclear fragmentation was performed using the chop and cylinder technique with 8.0 mJ of energy (spot and layer separation 9 μm each). A 2.4-mm temporal clear corneal incision was manually created using a slit knife. Cataract extraction with phacoemulsification was performed using the Centurion Vision System (Alcon Laboratories, Inc, Fort Worth, TX, USA). The trifocal diffractive IOL was placed in the center of the capsular bag. The second operation was performed 1 week after the first using the same procedure.

Examination of Tear Function, Ocular Surface Condition, Visual Acuity, Contrast Sensitivity with and Without Glare, and Disability Glare

TBUT, superficial punctate keratopathy in the central part of the cornea (C-SPK), high-order aberrations, and corrected distance visual acuity (CDVA) were checked at baseline (before initiation of dry eye treatment) and 1 week, 1 month, and 3 months after cataract operation. Fluorescein dye was used to evaluate ocular staining and TBUT. A fluorescein strip was wetted with saline, excess fluid was removed, and the fluorescein strip was applied to the inferior bulbar conjunctiva. The patients were instructed to blink a few times, TBUT was measured using a metronome, and the mean time (seconds) was calculated. Corneal staining in the center of the cornea was assessed using the National Eye Institute/Industry Workshop method [15]. The degree of C-SPK was scored from 0 to 3, where 0 = none, 1 = mild, 2 = moderate, and 3 = severe. The CASIA 2 (Tomey Corporation, Nagoya, Japan) was used to evaluate higher-order aberrations (HOAs) within a 4-mm area from the center of the cornea and provide a detailed model of the cornea's optical properties represented with Zernike polynomials. HOAs are combined values for the magnitude of the third- to sixth-order aberrations, calculated as the root-mean-square. CDVA was checked by the same qualified technician who performed the aforementioned evaluations using the Early Treatment Diabetic Retinopathy Study chart. Contrast sensitivity and disability glare were evaluated under mesopic conditions (background luminance 10 cd/m^2), with the contrast glare tester CGT-1000 (Takagi Seiko Co, Nagano, Japan). Contrast sensitivity was measured monocularly on the basis of six target ring sizes with and without glare using eight glare sources (Fig. 1). The targets were rings of variable sizes, situated at a distance of 35 cm from the screen, and the test was performed with near corrected vision. The target visual angles were 6.3, 4.0, 2.5, 1.6, 1.0, and 0.7 degrees (Fig. 2). The widths of the dark rings (2.9, 1.8, 1.2, 0.7, 0.5, and 0.3 mm) were used as target details for calculating the visual angles and cycles per degree (CPD). At a distance of 35 cm, these were compatible with visual angles of 28.6, 18.0, 11.4, 7.2, 4.5, and 2.9, with corresponding CPD of 1.1, 1.8, 2.9, 4.5, 7.1, and 10.4. Figure 2 shows the contrast threshold at 12 levels, ranging from 0.01 to 0.45, with and without glare at each visual angle of the targets. For statistical analysis, the contrast threshold was converted to log contrast sensitivity in this study. Disability glare was determined by analyzing the difference in contrast sensitivity with and without glare, which was also shown as log contrast sensitivity.

Statistical Analysis

All statistical analyses were performed using Excel statistical software package, version 3.21 (Bell Curve for Excel, Social Survey Research Information Co, Ltd, Tokyo, Japan). We used the post hoc power test to determine the power of our analysis. The Shapiro–Wilk test was used to examine if the numerical variables were normally distributed.

TBUT, C-SPK, HOAs, and CDVA at baseline were compared between the groups using the Mann–Whitney *U* test. After dry eye treatment, TBUT, C-SPK, HOAs, CDVA, contrast sensitivity

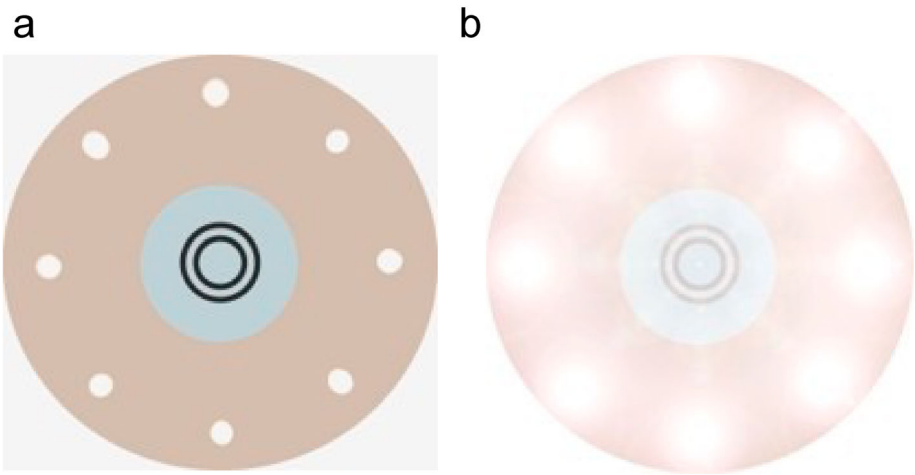

Fig. 1 Target rings without (**a**) and with glare (**b**)

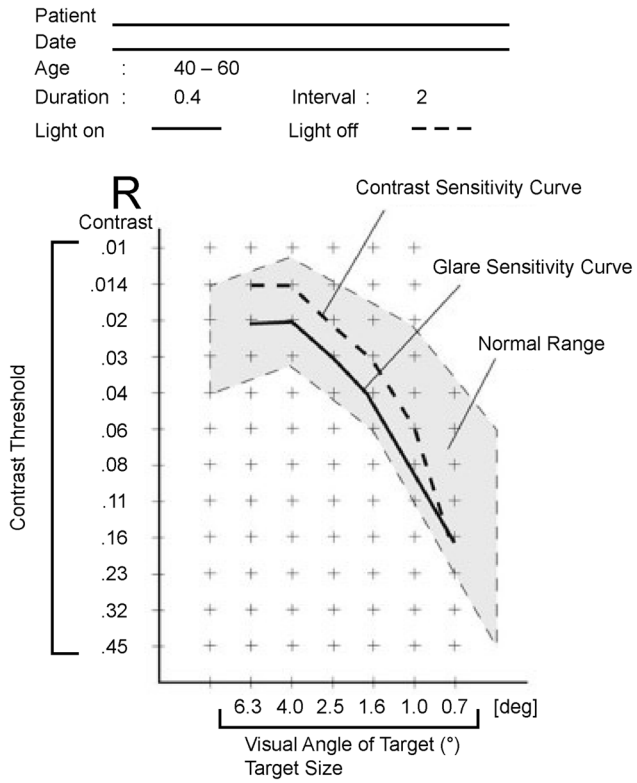

Fig. 2 Output data showing the contrast sensitivity with and without glare plotted against the visual angles of the whole targets

with and without glare, and disability glare at 1 week, 1 month, and 3 months after surgery were compared between groups R and A using the Mann–Whitney *U* test. Statistical significance was set at $p < 0.05$.

RESULTS

This study included 72 eyes of 36 patients (17 men and 19 women) with clinically diagnosed

dry eyes. The age of the patients ranged from 67 to 79 years (mean 73.6 ± 3.4 years).

The nurses confirmed that all patients followed the designated dry eye treatment protocol. Among the 36 patients, rebamipide was used in the right eye and artificial tears in the left eye of 18 patients, and vice versa for the other 18 patients. No adverse events related to cataract surgery or medications were reported during the investigation. The post hoc power test confirmed that the power of our analysis for the given sample size ($n = 36$) was 83% for a medium effect size ($d = 0.5$) and significance level of 0.05. Therefore, we considered the results of our research as indicative. According to the Shapiro–Wilk test, none of the numerical variables followed a normal distribution ($p < 0.05$). Therefore, we used the non-parametric Mann–Whitney *U* test to compare TBUT, C-SPK, HOAs, and CDVA between the groups.

Baseline

Table 1 shows the mean values (TBUT, C-SPK, HOAs, pupil size, and CDVA) at baseline in group R and group A. No significant difference was observed in the mean values at baseline between the two groups.

Table 1 Baseline data in group A and group R

	Mean ± SD		
	Group A	Group R	*p* value[a]
TBUT	3.72 ± 0.99	3.78 ± 1.00	0.509
C-SPK	0.36 ± 0.48	0.33 ± 0.47	0.732
HOAs	0.26 ± 0.04	0.25 ± 0.04	0.244
Pupil size	3.05 ± 0.15	3.05 ± 0.14	0.106
CDVA (logMAR)	0.40 ± 0.17	0.42 ± 0.16	0.552

SD standard deviation, *TBUT* tear breakup time, *C-SPK* superficial punctate keratopathy in the central cornea, *HOAs* higher-order aberrations, *CDVA* corrected distance visual acuity

[a]Mann–Whitney *U* test

Postoperative CDVA

Table 2 shows the mean CDVA at 1 week, 1 month, and 3 months postoperatively in groups R and A. The differences between the two groups were statistically significant at 1 week and 1 month ($p = 0.013$ and $p = 0.026$, respectively), but not significant at 3 months ($p = 0.063$), postoperatively.

Contrast Sensitivity and Disability Glare

Figures 3, 4, and 5 show contrast sensitivity without glare under mesopic conditions in group R and group A after 1 week, 1 month, and 3 months after surgery, respectively. The differences between the groups were statistically significant at all spatial frequencies at 1 week and 1 month postoperatively ($p < 0.001$). Statistically significant differences between the groups were observed at 1.1,1.8, 2.9, and 7.1 CPD ($p < 0.001$ [CPD = 1.1], $p < 0.05$ [CPD = 1.8, 2.9, and 7.1]), but these were not significant at CPD of 4.5 and 10.2, at 3 months postoperatively.

Figures 6, 7, and 8 show disability glare in group R and group A after 1 week, 1 month, and 3 months, respectively. The between-group differences were statistically significant at all spatial frequencies at 1 week and 1 month ($p < 0.001$). These differences were also statistically significant at CPD of 1.1, 2.9, 4.5, 7.1, and 10.2 ($p < 0.001$ [CPD = 1.1, 2.9, and 10.2], $p < 0.001$ [CPD = 4.5 and 7.1]), but were not

Table 2 Mean CDVA (logMAR) in group A and group R at 1 week, 1 month, and 3 months postoperatively

	Mean ± SD		
	Group A	Group R	*p* value[a]
1 week	0.13 ± 0.12	0.06 ± 0.09	0.013
1 month	0.05 ± 0.10	0.00 ± 0.07	0.026
3 months	0.00 ± 0.08	− 0.03 ± 0.05	0.063

SD standard deviation, *CDVA* corrected distance visual acuity

[a]Mann–Whitney *U* test

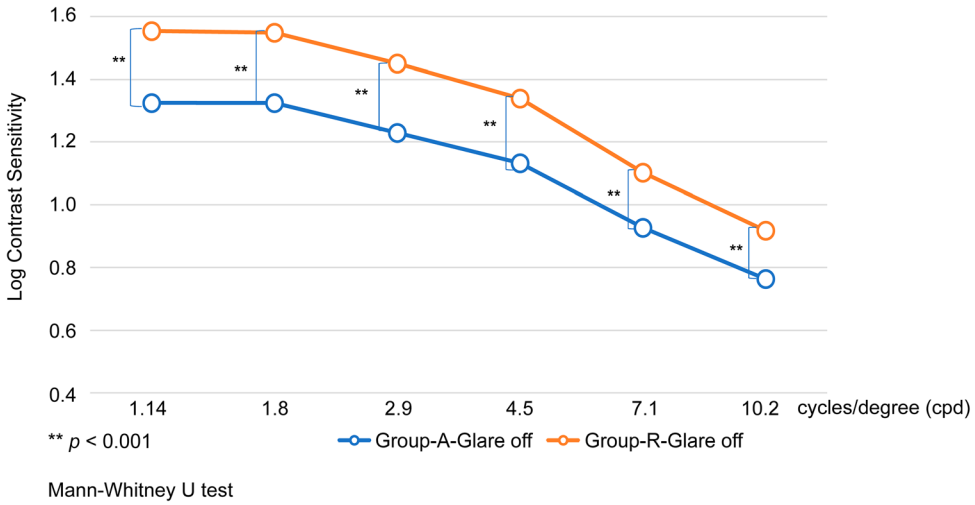

Fig. 3 Logarithm of contrast sensitivity without glare 1 week after operation

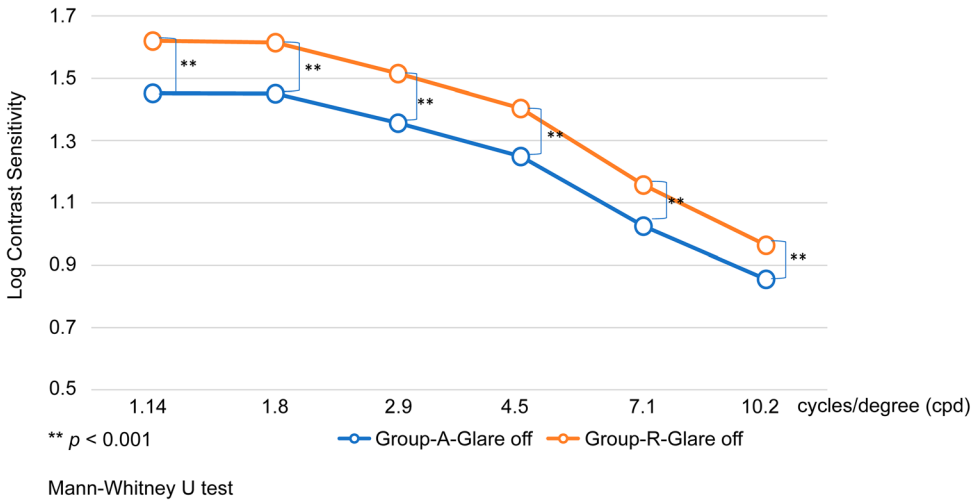

Fig. 4 Logarithm of contrast sensitivity without glare 1 month after operation

significant at a CPD of 1.8, at 3 months ($p < 0.001$) postoperatively.

Tear Film Stability

Table 3 shows the mean TBUT in group R and group A at 1 week, 1 month, and 3 months postoperatively. The TBUT was significantly longer in group R than in group A on each assessment day ($p < 0.001$).

Ocular Surface Condition

Table 4 shows the mean C-SPK in groups R and A at 1 week, 1 month, and 3 months postoperatively. The C-SPK was significantly lower in group R than in group A on each assessment day ($p < 0.001$).

Table 5 shows the mean HOAs in the two groups at 1 week, 1 month, and 3 months postoperatively. The HOAs in group R were significantly lower than those in group A on each assessment day ($p < 0.001$).

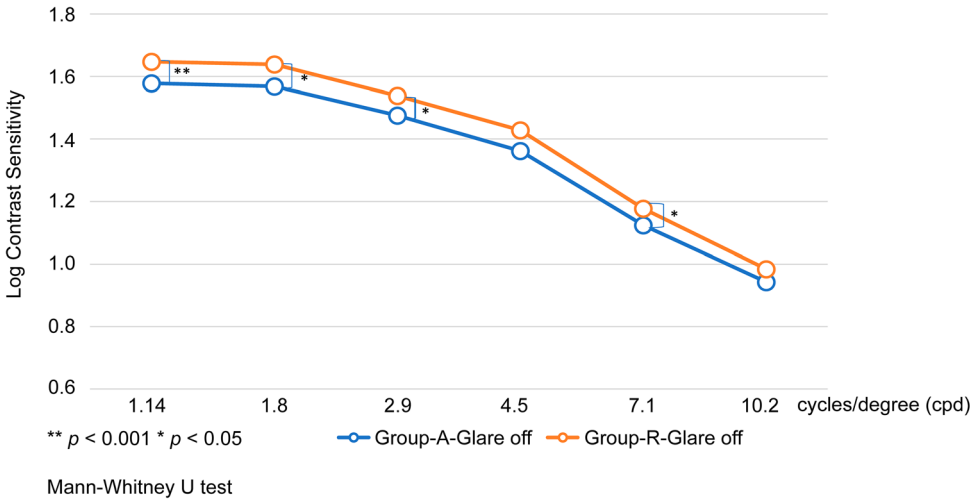

Fig. 5 Logarithm of contrast sensitivity without glare 3 months after operation

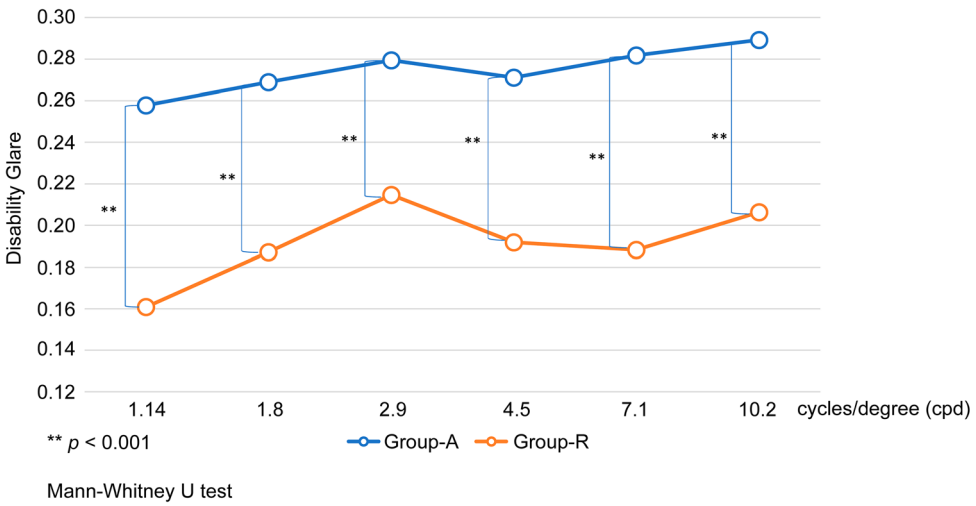

Fig. 6 Disability glare 1 week after operation

DISCUSSION

This study compared the effects of dry eye treatment with rebamipide versus artificial tears on ocular surface condition (TBUT, C-SPK, and HOAs) and quality of vision (CDVA, contrast sensitivity, and disability glare) during the perioperative period of cataract surgery with implantation of a diffractive trifocal IOL. Our findings suggest that rebamipide can help improve tear film stability, ocular surface condition, and quality of vision after cataract surgery with trifocal IOLs more than the artificial tears. These results further reveal that dry eye treatment with rebamipide during the perioperative period is effective in alleviating the negative effects of stress of a cataract operation on tear film stability. Additionally, it resulted in improved quality of the ocular surface, which led to an augmentation in the quality of vision with diffractive trifocal IOLs. In this study, we assessed the efficacy of dry eye treatment using a variety of clinical tests. While there have been similar studies in the past which have compared the effects of different types of eye drops, such as cyclosporine 0.05%, diquafosol ophthalmic

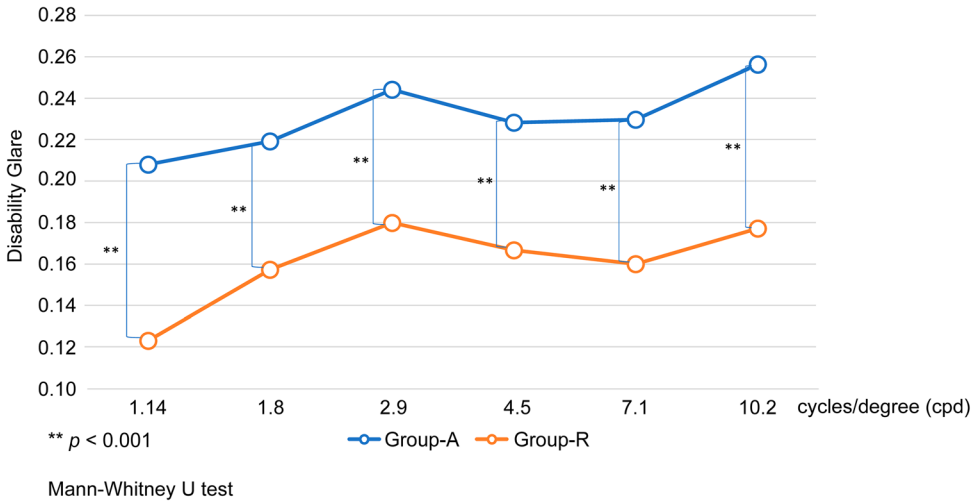

Fig. 7 Disability glare 1 month after operation

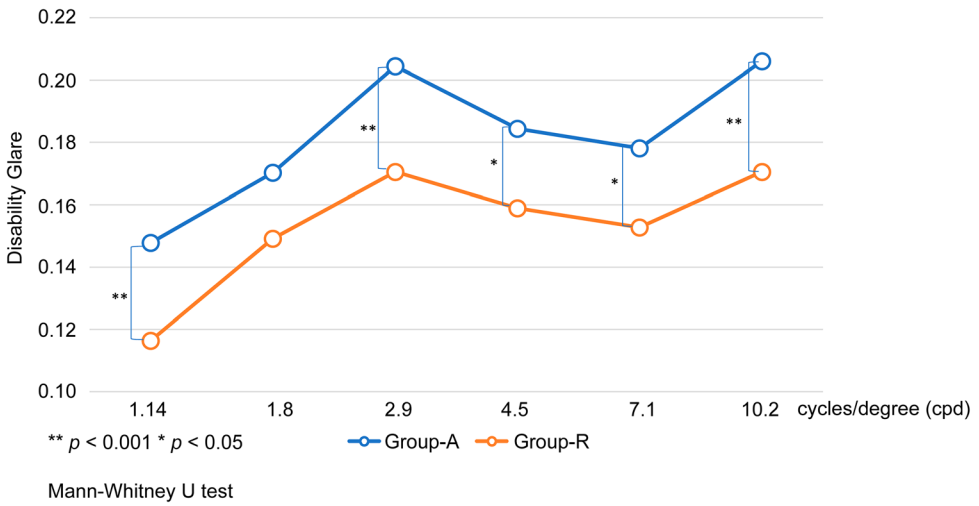

Fig. 8 Disability glare 3 months after operation

Table 3 Mean TBUT in group A and group R at 1 week, 1 month, and 3 months postoperatively

	Mean ± SD		
	Group A	**Group R**	***p* value[a]**
1 week	2.39 ± 1.03	3.89 ± 0.91	< 0.001
1 month	2.83 ± 1.12	4.39 ± 0.95	< 0.001
3 months	3.61 ± 1.06	5.17 ± 0.83	< 0.001

SD standard deviation, *TBUT* tear breakup time
[a]Mann–Whitney *U* test

Table 4 Mean C-SPK in group A and group R at 1 week, 1 month, and 3 months postoperatively

	Mean ± SD		
	Group A	**Group R**	***p* value[a]**
1 week	1.53 ± 0.96	0.50 ± 0.60	< 0.001
1 month	0.94 ± 0.81	0.17 ± 0.37	< 0.001
3 months	0.39 ± 0.54	0.08 ± 0.28	< 0.001

SD standard deviation, *C-SPK* superficial punctate keratopathy in central part of cornea
[a]Mann–Whitney *U* test

Table 5 HOAs in group A and group R at 1 week, 1 month, and 3 months postoperatively

	Mean ± SD		
	Group A	**Group R**	***p* value**[a]
1 week	0.37 ± 0.07	0.30 ± 0.05	< 0.001
1 month	0.33 ± 0.06	0.26 ± 0.04	< 0.001
3 months	0.28 ± 0.05	0.23 ± 0.03	< 0.001

SD standard deviation, *HOAs* higher order aberrations
[a]Mann–Whitney *U* test

solution, and artificial tears on postoperative quality of vision [16, 17], as far as we know, the present study is the first to indicate a significant positive effect of dry eye treatment with rebamipide in comparison to artificial tears, during the perioperative period of cataract surgery, on the postoperative quality of vision. Although the magnitude of statistically significant difference in some variables was relatively small, it is still imperative for eye doctors to acknowledge the clinical significance of these differences in order to compare the effectiveness of the two eye drops in a precise manner.

Previous studies have reported that cataract surgery can cause new episodes of dry eye or worsen preexisting dry eye [6, 18, 19]. The possible factors underlying this include sterilization, exposure to microscope light, use of antibiotic and anti-inflammatory eye drops, corneal incision, and surgically induced corneal inflammation, etc. [20, 21]. Ishrat et al. reported that 42% of eyes were diagnosed as dry eye 1 week after cataract operation, and the proportion decreased to 15% at 1 month and 9% at 3 months after operation [19]. Li et al. also demonstrated that while dry eyes without corneal staining 1 week after cataract operation improved by 3 months after surgery, it took longer than 3 months for dry eyes with corneal staining to show improvement without effective treatment [6]. Despite the fact that many patients acquire improved visual acuity after cataract surgery, some patients suffer from dry eye and reduced visual quality postoperatively. It is recognized that dry eye can decrease the quality of vision because of the instability of the tear film and irregularity of the surface of the cornea postoperatively [22, 23]. Koh et al. demonstrated that C-SPK is responsible for reducing contrast sensitivity in dry eye patients [3]. In their study, Huang et al. indicated that tear film instability may increase disability glare [11]. Szczotka-Flynn et al. also referred to the negative effect of dry eye on visual acuity and contrast sensitivity [24]. Furthermore, Tong et al. demonstrated the impact of dry eye on various vision-related daily activities [25]. Therefore, past research has indicated that there is a correlation between dry eye and a decrease in the quality of vision. These results highlight the importance of perioperative dry eye treatment.

In this study, we found that TBUT was significantly longer in group R than in group A, and C-SPK and HOAs in group R were significantly smaller than those in group A postoperatively. These results were comparable to those of a previous study, which demonstrated significant improvement in these variables with dry eye treatment using rebamipide during the perioperative period compared with the administration of artificial tears postoperatively; however, the type of artificial tears used was different from our study [12]. In addition, regarding the effect of dry eye treatment during the perioperative period on visual quality, in our study, CDVA and contrast sensitivity were significantly higher, and disability glare was significantly lower in group R than in group A. These trends were more remarkable during the early postoperative period. Therefore, we may be able to extrapolate that dry eye treatment with rebamipide during the perioperative period of cataract surgery may be more effective in improving tear film stability and ocular surface condition, which may enhance the quality of vision postoperatively compared with artificial tears. These deductions are supported by a few previous reports. Studies have shown a significant decrease in conjunctival goblet cell density after cataract surgery [6, 26]. Ríos et al. demonstrated that rebamipide had the ability to stimulate the proliferation of conjunctival goblet cells [27]. Kato et al. reported that rebamipide prevented the decrease in conjunctival goblet cell density due to cataract surgery [26].

There are some limitations to our study. The Japanese definition of dry eye was used in this study, which is different from the Dry Eye Workshop definition followed in western countries [28]. It was reported that short TBUT-type dry eye is more common in Japan and other Asian countries compared with the other types [29, 30]. Therefore, the Asia Dry Eye Society created a new definition and diagnostic criteria for dry eye to suit Asian populations [31]. It was also reported that the severity of symptoms and the severity of ocular surface damage signs in short TBUT-type dry eye are not always exactly correlated [31]. Further research including other definitions of dry eye is needed to investigate if alternative definitions could influence the results. Additionally, in this study, a basic four-point scale applied in the National Eye Institute/Industry Workshop method was used to assess C-SPK. Assessments with different scoring systems, such as the Oxford scaling [32], may also affect the findings. Moreover, there was a difference of 1 week between the two operations. There is a possibility that the ensuing difference in initiating the dry eye treatment could have affected the early postoperative outcomes. Furthermore, we only considered trifocal IOLs in our study and it would be interesting to perform the same investigation with monofocal IOLs. Recently, different types of dry eye treatments, such as intensive pulse light and thermal palpation system, have been introduced, and their effectiveness in management of dry eye condition has been reported [33, 34]. Therefore, a comparison of the effect of different types of dry eye treatments on the improvement of vision quality after cataract surgery may be of value.

CONCLUSIONS

Dry eye treatment with rebamipide during the perioperative period of cataract surgery with trifocal IOL implantation was more helpful than artificial tears in alleviating postoperative tear film instability and corneal surface irregularity. These factors resulted in further improvement in postoperative visual acuity, contrast sensitivity, and disability glare with rebamipide use. Thus, it can be concluded that dry eye treatment with rebamipide during the perioperative period may be able to improve patient satisfaction in cases with multifocal IOL implantation.

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Disclosures. Takeshi Teshigawara, Akira Meguro, and Nobuhisa Mizuki declare that they have no conflict of interest.

Compliance with Ethics Guidelines. This study received ethical approval from the committees of Yokosuka Chuo Eye Clinic and Tsurumi Chuo Eye Clinic (reference number 2021-003). The study was performed in accordance with the Helsinki Declaration of 1964, and its later amendments. Before starting the

research process, detailed information was provided, and written informed consent was obtained from all subjects to participate in this study and publish the resulting data.

Data Availability. Datasets are available as electronic supplementary material.

REFERENCES

1. Bethke W. IOL Survey: new lenses turn surgeons' heads. Rev Ophthalmol. 2021. https://www.reviewofophthalmology.com/article/iol-survey-new-lenses-turn-surgeons-heads. Accessed 2 Dec 2021.

2. Solomon R, Donnenfeld ED. Refractive intraocular lenses: multifocal and phakic IOLs. Int Ophthalmol Clin. 2006;46:123–43. https://doi.org/10.1097/00004397-200604630-00012.

3. Koh S, Maeda N, Ikeda C, et al. The effect of ocular surface regularity on contrast sensitivity and straylight in dry eye. Invest Ophthalmol Vis Sci. 2017;58:2647–51. https://doi.org/10.1167/iovs.17-21894.

4. Puell MC, Benítez-del-Castillo JM, Martínez-de-la-Casa J, et al. Contrast sensitivity and disability glare in patients with dry eye. Acta Ophthalmol Scand. 2006;84:527–31. https://doi.org/10.1111/j.1600-0420.2006.00671.x.

5. Trattler WB, Majmudar PA, Donnenfeld ED, McDonald MB, Stonecipher KG, Goldberg DF. The prospective health assessment of cataract patients' ocular surface (PHACO) study: the effect of dry eye. Clin Ophthalmol. 2017;11:1423–30. https://doi.org/10.2147/OPTH.S120159.

6. Li XM, Hu L, Hu J, Wang W. Investigation of dry eye disease and analysis of the pathogenic factors in patients after cataract surgery. Cornea. 2007;26(Suppl 1):S16–20. https://doi.org/10.1097/ICO.0b013e31812f67ca.

7. Ram J, Gupta A, Brar GS, Kaushik S, Gupta A. Outcomes of phacoemulsification in patients with dry eye. J Cataract Refract Surg. 2002;28:1386–9. https://doi.org/10.1016/s0886-3350(02)01387-1.

8. Koh S, Maeda N, Hori Y, et al. Effects of suppression of blinking on quality of vision in borderline cases of evaporative dry eye. Cornea. 2008;27:275–8. https://doi.org/10.1097/ICO.0b013e31815be9c8.

9. Urashima H, Okamoto T, Takeji Y, Shinohara H, Fujisawa S. Rebamipide increases the amount of mucin-like substances on the conjunctiva and cornea in the *N*-acetylcysteine-treated in vivo model. Cornea. 2004;23:613–9. https://doi.org/10.1097/01.ico.0000126436.25751.fb.

10. Teshigawara T, Meguro A, Mizuki N. The effect of rebamipide on refractive accuracy of cataract surgery in patients with dry eye. Ophthalmol Ther. 2022;11:603–11. https://doi.org/10.1007/s40123-022-00457-3.

11. Huang FC, Tseng SH, Shih MH, Chen FK. Effect of artificial tears on corneal surface regularity, contrast sensitivity, and glare disability in dry eyes. Ophthalmology. 2002;109:1934–40. https://doi.org/10.1016/s0161-6420(02)01136-3.

12. Inoue Y, Ochi S, Koh S. Effect of 2% rebamipide ophthalmic suspension on perioperative period of cataract surgery in dry eye patients. Atarasii Ganka (J Eye). 2016;33:1363–8 (in Japanese).

13. Shimazaki J. Concept of new definition and diagnostic criteria of dry eye disease in 2016. Atarashii Ganka. 2018;35:853–7 (in Japanese).

14. Midorikawa-Inomata A, Inomata T, Nojiri S, et al. Reliability and validity of the Japanese version of the Ocular Surface Disease Index for dry eye disease. BMJ Open. 2019;9: e033940. https://doi.org/10.1136/bmjopen-2019-033940.

15. Lemp MA. Report of the National Eye Institute/industry workshop on clinical trials in dry eyes. CLAO J. 1995;21:221–32.

16. Donnenfeld ED, Solomon R, Roberts CW, Wittpenn JR, McDonald MB, Perry HD. Cyclosporine 0.05% to improve visual outcomes after multifocal intraocular lens implantation. J Cataract Refract Surg. 2010;36:1095–100. https://doi.org/10.1016/j.jcrs.2009.12.049.

17. Inoue Y, Ochi S. Effects of 3% diquafosol sodium ophthalmic solution on higher-order aberrations in patients diagnosed with dry eye after cataract surgery. Clin Ophthalmol. 2016;11:87–93. https://doi.org/10.2147/OPTH.S122542.

18. Roberts CW, Elie ER. Dry eye symptoms following cataract surgery. Insight (American Society of Ophthalmic Registered Nurses). 2007;32:14–23.

19. Ishrat S, Nema N, Chandravanshi SCL. Incidence and pattern of dry eye after cataract surgery. Saudi J Ophthalmol. 2019;33:34–40. https://doi.org/10.1016/j.sjopt.2018.10.009.

20. Sutu C, Fukuoka H, Afshari NA. Mechanisms and management of dry eye in cataract surgery patients. Curr Opin Ophthalmol. 2016;27:24–30. https://doi.org/10.1097/ICU.0000000000000227.

21. Cho YK, Kim MS. Dry eye after cataract surgery and associated intraoperative risk factors. Korean J Ophthalmol. 2009;23:65–73. https://doi.org/10.3341/kjo.2009.23.2.65.

22. Goto E, Ishida R, Kaido M, et al. Optical aberrations and visual disturbances associated with dry eye. Ocul Surf. 2006;4:207–13. https://doi.org/10.1016/s1542-0124(12)70167-2.

23. Goto E, Yagi Y, Matsumoto Y, Tsubota K. Impaired functional visual acuity of dry eye patients. Am J Ophthalmol. 2002;133:181–6. https://doi.org/10.1016/s0002-9394(01)01365-4.

24. Szczotka-Flynn LB, Maguire MG, Ying GS, et al. Impact of dry eye on visual acuity and contrast sensitivity: dry eye assessment and management study. Optom Vis Sci. 2019;96:387–96. https://doi.org/10.1097/OPX.0000000000001387.

25. Tong L, Waduthantri S, Wong TY, et al. Impact of symptomatic dry eye on vision-related daily activities: the Singapore Malay Eye Study. Eye (Lond). 2010;24:1486–91. https://doi.org/10.1038/eye.2010.67.

26. Kato K, Miyake K, Kondo N, et al. Conjunctival goblet cell density following cataract surgery with diclofenac versus diclofenac and rebamipide: a randomized trial. Am J Ophthalmol. 2017;181:26–36. https://doi.org/10.1016/j.ajo.2017.06.016.

27. Ríos JD, Shatos M, Urashima H, Tran H, Dartt DA. OPC-12759 increases proliferation of cultured rat conjunctival goblet cells. Cornea. 2006;25:573–81. https://doi.org/10.1097/01.ico.0000208819.24990.0d.

28. DEWS Definition and Classification Subcommittee. 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;5:75–92. https://doi.org/10.1016/s1542-0124(12)70081-2.

29. Kawashima M, Yamada M, Suwaki K, et al. A clinic-based survey of clinical characteristics and practice pattern of dry eye in Japan. Adv Ther. 2017;34:732–43. https://doi.org/10.1007/s12325-017-0487-x.

30. Uchino M, Yokoi N, Uchino Y, et al. Prevalence of dry eye disease and its risk factors in visual display terminal users: the Osaka study. Am J Ophthalmol. 2013;156:759–66. https://doi.org/10.1016/j.ajo.2013.05.040.

31. Tsubota K, Yokoi N, Shimazaki J, et al. New perspectives on dry eye definition and diagnosis: a consensus report by the Asia dry eye society. Ocul Surf. 2017;15:65–76. https://doi.org/10.1016/j.jtos.2016.09.003.

32. Bron AJ, Evans VE, Smith JA. Grading of corneal and conjunctival staining in the context of other dry eye tests. Cornea. 2003;22:640–50. https://doi.org/10.1097/00003226-200310000-00008.

33. Vigo L, Giannaccare G, Sebastiani S, Pellegrini M, Carones F. Intense pulsed light for the treatment of dry eye owing to meibomian gland dysfunction. J Vis Exp. 2019. https://doi.org/10.3791/57811.

34. Kim MJ, Stinnett SS, Gupta PK. Effect of thermal pulsation treatment on tear film parameters in dry eye disease patients. Clin Ophthalmol. 2017;11:883–6. https://doi.org/10.2147/OPTH.S136203.