Changes in Tear Osmolarity after Cataract Surgery

Tsutomu Igarashi\textsuperscript{1}, Hisatomo Takahashi\textsuperscript{2}, Maika Kobayashi\textsuperscript{1}, Tomoyuki Kunishige\textsuperscript{1}, Takeshi Arima\textsuperscript{1}, Chiaki Fujimoto\textsuperscript{1}, Hisaharu Suzuki\textsuperscript{1}, Takahisa Okuda\textsuperscript{3} and Hiroshi Takahashi\textsuperscript{1}

\textsuperscript{1}Department of Ophthalmology, Nippon Medical School, Tokyo, Japan
\textsuperscript{2}Department of Ophthalmology, Omagari Kousei Medical Center, Akita, Japan
\textsuperscript{3}Division of Legal Medicine, Department of Social Medicine, Nihon University School of Medicine, Tokyo, Japan

\textbf{Background:} The purpose of this study was to examine changes in the ocular surface before and after phacoemulsification with small incisions and to examine the changes in tear osmolarity.

\textbf{Methods:} This was a prospective, observational study involving 55 eyes of 39 patients (19 male, 20 female patients; average age 72.0±7.3 years) who had cataract surgery at a Nippon Medical School Hospital between December 2013 and June 2018. Compromised tear dynamics were determined by the Schirmer test or the tear break-up time (BUT). An abnormal ocular surface was identified by positive vital staining with fluorescein or lissamine green. Moreover, tear osmolarity (Tosm) and corneal sensitivity were measured. All assessments were done preoperatively and 1 and 4 weeks (P1W and P4W) after the surgery.

\textbf{Results:} None of the operations had any complications. Operating time was 17.8±9.3 minutes. BUT was significantly decreased at P1W, and it recovered at P4W. The Schirmer test did not change significantly. The fluorescein staining score (FSS) increased significantly at P1W and recovered at P4W. The Lissamine green score (LSS) did not change significantly. Tear osmolarity increased significantly at P1W and did not recover at P4W. Corneal sensitivity decreased significantly at P1W and recovered at P4W.

\textbf{Conclusion:} In the present study, there were temporary changes in dry eye-related examinations including tear osmolarity after cataract surgery. In particular, tear osmolarity increased significantly 4 weeks after surgery compared to before surgery, and it showed long-term changes, unlike other factors. After cataract surgery, tear osmolarity, BUT, and FSS increase, resulting in dry eye symptoms. Therefore, it is necessary to pay attention to uncomfortable eye symptoms of patients after cataract surgery.

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\textbf{Key words:} dry eye, tear osmolarity, cataract surgery, phacoemulsification

\textbf{Introduction}

According to the definition of dry eye in the 1995 National Eye Institute (NEI) / Industry Dry Eye Workshop, dry eye is defined as a chronic disease of tears and keratoconjunctival epithelium due to various factors, with eye discomfort and visual function disorders\textsuperscript{1}. In addition, the 2007 Dry Eye Work Shop (DEWS) report pointed out the importance of increased tear osmolarity and ocular surface inflammation for dry eye\textsuperscript{2}. The epidemiology sub-committee of the International Dry Eye Workshop (2007) reported that there were many studies citing aging as a crucial risk factor for dry eye\textsuperscript{3}. Aging causes cataracts in many people, and many patients with cataracts undergo phacoemulsification in developed countries. Since postoperative dry eye contributes to postoperative pain, diagnosis and treatment of the postoperative eye surface is important\textsuperscript{4}. Laser in Situ Keratomileusis (LASIK) is known to cause the most dry eye symptoms\textsuperscript{5} and increase the tear osmolarity\textsuperscript{6} after ophthalmic surgery, but cataract surgery has also been suggested to be a cause of
postoperative dry eye symptoms. Eye drops used postoperatively can cause dry eye. Phacoemulsification has been shown to reduce tear meniscus height, tear breakup time (BUT), and corneal sensitivity, decrease goblet cell density, and promote squamous metaplasia in conjunctival impression cytology. Several factors such as increased inflammatory mediators due to postoperative inflammation, toxicity due to the use of eye drops containing benzalkonium chloride, toxicity due to light exposure of operating microscope and damage to corneal sensory nerves can be considered related to the mechanism of deterioration of the condition of the ocular surface after cataract surgery.

The purpose of this study was to examine changes in the ocular surface before and after phacoemulsification in small incisions, which are common in developed countries, and to examine the changes in tear osmolarity, a new dry eye parameter.

Materials and Methods

Study Population

This was a prospective, observational study that followed the tenets of the Declaration of Helsinki and was approved by the Drug Ethics Committee of the Nippon Medical School Hospital (ID#225004). Informed consent was obtained in writing from all of the patients. Before subjects were enrolled, the study was registered at the Japanese University Hospital Medical Information Network Clinical Trials Registry (clinical trial identifier: UMIN 000111112; accessed 2013/07/03).

A total of 55 eyes of 39 patients (19 male and 20 female patients; average age 72.0 ± 7.3 years; range, 52 - 84 years) who had cataract surgery at Nippon Medical School Hospital between December 2013 and June 2018 were evaluated. None of the patients had a history of ocular surface diseases preoperatively or surgical complications after surgery by one surgeon (T.I.). Inclusion criteria are those who have agreed to clinical research and who can continue to visit our hospital for 4 weeks after surgery. Excluded from the study were contact lens wearers, patients with diabetes or pterygia, and eye drop users, including dry eye patients and glaucoma patients, patients with nuclear color grade 5 or more according to the Lens Opacities Classification System III (LOC III) classification and patients with severe ophthalmic disease such as corneal dystrophy, degenerative retinal diseases, and uveitis.

Cataract Surgery

Before cataract surgery, 1.5% levofloxacin (Santen Pharmaceutical Co. Ltd. Osaka, Japan) eye drop was instilled 4 times daily for 1 day. Tropicamide and phenylephrine hydrochloride (Santen Pharmaceutical Co. Ltd.) eye drop was used 3 times over half an hour to dilate the pupils before cataract surgery. Topical anesthesia was achieved with 0.4% oxybuprocaine hydrochloride (Santen Pharmaceutical Co. Ltd) and 4% lidocaine (AstraZeneca K.K, Osaka, Japan). After inflating the capsular bag with Opegan High, a foldable intraocular lens (iSert Micro 255; Hoya Surgical Optics, Tokyo, Japan) was implanted. Both of these incisions were self-healing. The operation time was recorded. Postoperative management of the patients included 1% betamethasone sodium phosphate (Shionogi, Osaka, Japan) and 1.5% revofloxin (Santen Pharmaceutical Co. Ltd) four times a day and 0.1% bromfenac sodium two times a day for 4 weeks.

Clinical Evaluation of Dry Eye

Compromised tear dynamics were determined by the Schirmer test or the BUT. An abnormal ocular surface was identified by positive vital staining with fluorescein or lissamine green. Moreover, tear osmolarity (Tosm) was measured using the Tearlab system (Tearlab, San Diego, CA), and corneal sensitivity was measured using a Cochet-Bonnet aesthesiometer (Richmond Products, Albuquerque, NM). All assessments were done preoperatively and postoperatively at 1 and 4 weeks after the surgery.

Statistical Analysis

In this experiment, each result was calculated for each eye, not for each patient. The means and standard deviations (SDs) of these measurements were calculated for each group. Regarding the statistical analysis, Student-Newman-Keuls (SNK) methods was performed for a significant difference between factors in the case of a significant difference in repeated measures ANOVA (Excel; Microsoft, Tokyo, Japan). A p value of <0.05 was considered significant.
Figs. 1 A Each parameter of dry eye (DE). All parameters are compared preoperatively, and at 1 and 4 weeks postoperatively. (A) Tear break-up time (BUT), (B) Schirmer test, (C) fluorescein staining score (FSS), (D) Lissamine green score (LSS), (E) Tear osmolarity, (F) Corneal sensitivity. (**p<0.01, *p<0.05)

Results

None of the operations had any complications. Operating time was 17.8±9.3 minutes. All assessment parameters were obtained preoperatively and at 1 and 4 weeks after the surgery (P1W and P4W) (Table 1). BUT was significantly decreased at P1W, and it recovered at P4W (Fig. 1A). The Schirmer test did not change significantly (Fig. 1B). The fluorescein staining score (FSS) increased significantly at P1W and recovered at P4W (Fig. 1C). The Lissamine green score (LSS) did not change significantly (Fig. 1D). Tear osmolarity increased significantly at P1W and did not recover at P4W (Fig. 1E). Corneal sensitivity decreased significantly at P1W and recovered at P4W (Fig. 1F).

Discussion

Previous reports of dry eye before and after cataract surgery stated that BUT and corneal sensitivity were most aggravated on the first day after surgery and improved to the same level as before surgery one month later8,9. On the Schirmer test, one study found that there was no significant difference between before and after surgery8, and another study showed that the tear dynamics recovered within one month after surgery9. The present results showed similar trends to those previously reported. Tear osmolarity can be an objective examination for diagnosing dry eye20-23. There is a correlation between tear osmolarity above 316 mOsm/L and dry eye, and tear osmolarity was the only quantifiable factor in the DEWS report24. However, few have reported a high correlation between high tear osmolarity and dry eye. In our previous study, the tear osmolarity of dry eye was 288 mOsm/L, which was not different from that of normal people18. The present study focused on dry eye after cataract surgery and

Table 1 Profiles of parameters

| Characteristic                | Pre-ope | 1W post ope | 4W post ope |
|------------------------------|---------|-------------|-------------|
| Tear function                |         |             |             |
| Break-up time (BUT)          | 4.6 ± 1.9 | 4.1 ± 2.0   | 4.6 ± 2.6   |
| Schirmer test (SCH)          | 10.2 ± 7.0 | 9.0 ± 7.5   | 9.1 ± 5.9   |
| Ocular surface condition     |         |             |             |
| Fluorescein score (FSS)      | 0.3 ± 0.8 | 0.5 ± 1.1   | 0.3 ± 0.8   |
| Lissamine Green score (LSS)  | 0.3 ± 1.0 | 0.4 ± 0.9   | 0.3 ± 0.8   |
| Tear osmolarity (Tosm)       | 286.4 ± 8.3 | 290.9 ± 10.0  | 289.0 ± 8.8 |
| Corneal sensitivity (CS)     | 5.7 ± 0.5 | 5.5 ± 0.7   | 5.7 ± 0.5   |
evaluated changes in tear osmolarity before and after cataract surgery. It was found that tear osmolarity increased significantly 1 week after surgery (p < 0.01) and remained significantly elevated 4 weeks later compared to preoperatively (p < 0.01) (Fig. 1E). Elknsis et al reported that tear osmolarity increased significantly at the first week after surgery, but it decreased to the preoperative level four weeks after surgery. However, González-Mesa et al reported no differences in tear osmolarity between before and after the operation. In this experiment, the reason why the tear osmolarity changed before and after the operation was not considered to be due to the change in tear volume, because no change was seen on the Schirmer test. It is thought that postoperative inflammation led to an increase in tear osmolarity.

But was examined as a parameter of tear film stability, but it decreased significantly 1 week after surgery (p < 0.05) and returned to the same level as before surgery after 4 weeks (Fig. 1A).

The recovery period of postoperative corneal sensitivity ranges from 3 weeks to 9 months in LASIK and 3 months for refractive keratotomy. Microincision surgery such as phacoemulsification is considered less likely to cause a decrease in corneal sensitivity than refractive surgery or extracapsular cataract extraction. In cataract surgery, the loss of corneal sensitivity depends on the size of the incision. Kohlhaas M et al reported that using a 7 mm incision, corneal sensitivity did not return after 12 months. Khanal S et al reported that using a 4.1 mm incision, it did not return after 3 months. Oh T et al reported that using a 2.8 mm incision, it returned after one month. In our experiment, it returned after one month using a 2.4 mm incision. The decrease in corneal sensitivity after ocular surgery is thought to be due to the corneal incision size. Since the corneal sensitivity of 2.8 mm incision decreased from 58.6 mm to 52.3 mm (89%) after 1 week and 2.4 mm incision decreased from 57.1 mm to 55.2 mm (96%) after 1 week, a smaller incision may have less effect on corneal sensitivity.

In the present study, there were temporary changes in dry eye-related examinations including tear osmolarity after cataract surgery. In particular, tear osmolarity increased significantly 4 weeks after surgery compared to preoperative levels, and it showed long-term changes, unlike other factors. The transient increase in tear osmolarity, an important factor for dry eye in the DEWS report, was confirmed by cataract surgery that caused dry eye.

**Conflict of Interest:** The authors declare no conflict of interest.

**References**

1. Lemp MA. Report of the National Eye Institute/Industry workshop on clinical trials in dry eyes. CLAO J. 1995 Oct; 21(4):221–32.
2. 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 Apr;5(2):75–92.
3. The epidemiology of dry eye disease: report of the Epidemiology Subcommittee of the International Dry Eye Workshop (2007). Ocul Surf. 2007 Apr;5(2):93–107.
4. Porela-Tihonen S, Kaarniranta K, Kokki H. Postoperative pain after cataract surgery. J Cataract Refract Surg. 2013 May;39(5):789–98.
5. Albiez JM, Lenton LM. Management of the ocular surface and tear film before, during, and after laser in situ keratomileusis. J Refract Surg. 2004 Jan-Feb;20(1):62–71.
6. Kacerovsky J, Kacerovsky M, Hlavackova M, Studeny P. Change of tear osmolarity after refractive surgery. Cesk Slov Oftalmol. 2018;74(1):18–22.
7. Cho YK, Kim MS. Dry eye after cataract surgery and associated intraoperative risk factors. Korean J Ophthalmol. 2009 Jun;23(2):65–73.
8. 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 Mar;56(2):113–8.
9. Khanal S, Tomlinson A, Esakovitz L, et al. Changes in corneal sensitivity and tear physiology after phacoemulsification. Ophthalmic Physiol Opt. 2008 Mar;28(2):127–34.
10. 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 Oct;26(9 Suppl 1):S16–20.
11. Ram J, Gupta A, Brar G, Kaushik S, Gupta A. Outcomes of phacoemulsification in patients with dry eye. J Cataract Refract Surg. 2002 Aug;28(8):1386–9.
12. Jung JW, Han SJ, Nam SM, Kim TI, Kim EK, Seo KY. Meibomian Gland Dysfunction (MGD) and Tear Cytokines after Cataract Surgery according to Preoperative Meibomian Gland Status. Clin Exp Ophthalmol. 2016 Sep;44(7):555–62.
13. Epstein SP, Chen D, Asbell PA. Evaluation of biomarkers of inflammation in response to benzalkonium chloride on corneal and conjunctival epithelial cells. J Ocul Pharmacol Ther. 2009 Oct;25(5):415–24.
14. Hwang HB, Kim HS. Phototoxic effects of an operating microscope on the ocular surface and tear film. Cornea. 2014 Jan;33(1):82–90.
15. Ipek T, Hanga MP, Hartwig A, Wolfsohn J, O’Donnell C. Dry eye following cataract surgery: The effect of light exposure using an in-vitro model. Cont Lens Anterior Eye. 2018 Feb;41(1):128–31.
16. Igarashi T, Ohsawa I, Kobayashi M, et al. Effects of hydrogen in prevention of corneal endothelial damage during phacoemulsification: A prospective randomized clinical trial. Am J Ophthalmol. 2019 Nov;207:10–7.
17. Igarashi T, Fujita M, Yamada Y, et al. Improvements in signs and symptoms of dry eye after instillation of 2% rebamipide. J Nippon Med Sch. 2015;82(5):229–36.
18. Kobayashi M, Igarashi T, Takahashi H, Fujimoto C, Suzuki H, Takahashi H. The correlation between plasma
osmolarity and tear osmolarity. Int Ophthalmol. 2017 Apr;38(2):493–501.
19. Igarashi T, Ono M, Fujimoto C, Suzuki H, Takahashi H. The conjunctival sensitivity in soft contact lens wearers. Int Ophthalmol. 2015 Aug;35(4):569–73.
20. Farris RL, Gilbard JP, Stuchell RN, Mandel ID. Diagnostic tests in keratoconjunctivitis sicca. CLAO J. 1983 Jan-Mar;9(1):23–8.
21. Gilbard JP, Farris RL, Santamaria J 2nd. Osmolarity of tear microvolumes in keratoconjunctivitis sicca. Arch Ophthalmol. 1978 Apr;96(4):677–81.
22. Mathers WD, Lane JA, Sutphin JE, Zimmerman MB. Model for ocular tear film function. Cornea. 1996 Mar;15(2):110–9.
23. Sullivan BD, Whitmer D, Nichols KK, et al. An objective approach to dry eye disease severity. Invest Ophthalmol Vis Sci. 2010 Dec;51(12):6125–30.
24. Tomlinson A, Khanal S, Ramaesh K, Diaper C, McFadyen A. Tear film osmolarity: determination of a referent for dry eye diagnosis. Invest Ophthalmol Vis Sci. 2006 Oct;47(10):4309–15.
25. Elknsis E, Lace I, Laganovska G, Erts R. Tear osmolarity after cataract surgery. J Curr Ophthalmol. 2019 Mar;31(1):31–5.
26. Gonzalez-Mesa A, Moreno-Arrones JP, Ferrari D, Teus MA. Role of tear osmolarity in dry eye symptoms after cataract surgery. Am J Ophthalmol. 2016 Oct;170:128–32.
27. Nassaralla BA, McLeod SD, Nassaralla JJ Jr. Effect of myopic LASIK on human corneal sensitivity. Ophthalmology. 2003 Mar;110(3):497–502.
28. Perez-Santonja JJ, Sakla HF, Cardona C, Chipont E, Alia JL. Corneal sensitivity after photorefractive keratectomy and laser in situ keratomileusis for low myopia. Am J Ophthalmol. 1999 May;127(5):497–504.
29. Matsui H, Kumano Y, Zushi I, Yamada T, Matsui T, Nishida T. Corneal sensation after correction of myopia by photorefractive keratectomy and laser in situ keratomileusis. J Cataract Refract Surg. 2001 Mar;27(3):370–3.
30. Hoffman RS, Fine IH, Packer M. New phacoemulsification technology. Curr Opin Ophthalmol. 2005 Feb;16(1):38–43.
31. Kohlhaas M, Stahlhut O, Tholuck J, Richard G. Entwicklung der Hornhautsensibilität nach Phakoemulsifikation mit skleralem Tunnelschnitt [Development of corneal sensitivity after phacoemulsification with scleral tunnel incision]. Klin Monbl Augenheilkd. 1997 Jul;211(1):32–6. German.
32. Lyne A. Corneal sensitivity after surgery. Trans Ophthalmol Soc U K. 1982 Jul;102(pt 2):302–5.

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