Original research

Photorefractive keratectomy for patients with preoperative low Schirmer test value

Elham Tanbakouee a, Mohammad Ghoreishi b, Mohammad Aghazadeh-Amiri a,*, Mehdi Tabatabae c, Mohadeseh Mohamadinia d

* Department of Optometry, School of Rehabilitation, Shahid Beheshti University of Medical Sciences, Tehran, Iran
b Ophthalmology Department, Isfahan University of Medical Sciences, Isfahan, Iran
c Department of Basic Sciences, School of Rehabilitation, Shahid Beheshti University of Medical Sciences, Tehran, Iran
d Research and Development Department, Persian Eye Clinic, Isfahan, Iran

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Abstract

Purpose: To compare dry eye signs and symptoms between patients with preoperative low and normal Schirmer test after Photorefractive keratectomy (PRK).

Methods: In this prospective, nonrandomized, comparative case series, 76 eyes of 76 patients were preoperatively categorized into two groups according to selected criteria for characterization of tear film status: the low Schirmer test value (STV) group and the normal STV group. For the tear function assessment, we performed a Schirmer test with and without anesthesia, tear break-up time (TBUT) test, and measurement dry eye symptoms using the Farsi translation of Ocular Surface Disease Index (OSDI) questionnaire pre- and 3 months post-operation.

Results: Postoperatively, the Schirmer and TBUT values were significantly lower in both groups than preoperatively (all p < 0.05). Deterioration in tear secretion was significantly greater in the low STV group (p = 0.012), but tear stability was more compromised in the normal STV group (p = 0.021). The changes in OSDI score were not significant between the two groups.

Conclusion: These results demonstrated that tear function deteriorates after PRK. Therefore, patients with low preoperative Schirmer test values should be thoroughly assessed for dry eye before proceeding with refractive surgery to eliminate postoperative complication.

Keywords: Schirmer test; Photorefractive keratectomy; Tear function

Introduction

Dry eye is one of the most common reported and observed findings in the short-term following photorefractive procedures.1–10 Although it is usually transient, some patients complain of severe symptoms, which may negatively influence the quality of life and their satisfaction with the outcome of the procedure.11–15

The pathophysiologic mechanisms behind post-photorefractive surgery dry eye have been previously reviewed, and several hypotheses have been proposed.16–18 Photorefractive surgery compromises the corneal sensory nerve, resulting in impaired corneal sensation. Decreased afferent input to the lacrimal functional unit results in decreased tear secretion, leading to a deficient aqueous component of the tear film.

Furthermore, according to some previous studies, pre-existing dry eye disease is a major risk factor for severe post-operative dry eye with lower tear function and more

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severe symptoms. Preoperative Schirmer score is of particular importance, and its preoperative value has been reported to statistically significantly correlate with postoperative dry eye symptoms. Few studies exist in literature investigating the effect of preoperative tear function on development of postoperative dry eye sign and symptoms. It is uncertain if preoperative Schirmer test value (STV) is a predictive factor for the development of more dry eye symptoms after surgery.

In this study, we compare the objectively-measured clinical signs and subjective reporting of dry eye symptoms between two groups of patients who underwent photorefractive keratotomy (PRK) over a period of 3 months.

Methods

In this prospective, nonrandomized, comparative case series study, 76 eyes of 76 patients (46 female, 30 male) with low-to-moderate myopia and astigmatism who were scheduled for PRK in Persian Eye Clinic were enrolled. One eye (right eye) from each patient was included. The research followed the tenets of the Declaration of Helsinki, and informed consent was obtained from all subjects. The study protocol was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences.

The eyes were divided into the following 2 groups on the basis of preoperative tear secretion: eyes with low Schirmer test value (low STV group; 36 patients and 36 eyes) and normal Schirmer test value (normal STV group; 40 patients and 40 eyes). Results of Schirmer 1 test were used as selected criteria for classification of patients. The eyes with Schirmer test values between 5 and 10 mm were considered for the low STV group, and eyes with Schirmer test values > 10 mm were considered for the normal STV group. Patients who had any contraindication of corneal refractive surgery and/or severe signs and symptoms of dry eye were excluded from the study.

All patients had a complete ophthalmic examination including uncorrected and corrected distance visual acuity (UDVA and CDVA), manifest and cycloplegic refraction, slit lamp microscopy, corneal topography and pachymetry (Pentacam HD, Oculus Optikgerate GmbH, Wetzlar, Germany), indirect ophthalmoscopy, and tear film function assessment.

To assess tear function, all patients completed the Farsi translation of Ocular Surface Disease Index (OSDI) questionnaire and underwent examination of tear secretion with Schirmer test (with and without anesthesia) and tear film stability with TBUT test prior and 3 months after surgery.

Schirmer test was performed without anesthesia (Schirmer 1) and also with anesthesia 5 min after instilling one drop of tetracaine 0.5% into the conjunctival sac (Schirmer 2) for test the paper strips (OPHTECHNICS UNLIMITED, India) were placed over the junction of the temporal and medial one-third of the lower eyelid margin. The eyes were closed during the test, and the length of the wet portion was measured.

TBUT was assessed with fluorescein paper strips that were wetted with unpreserved saline solution. One drop was instilled in each eye in the lower conjunctival sac, and the patient was instructed to blink several times. The tear BUT was measured as the number of seconds between the last complete blink and the first sign of break in the precorneal tear film. The TBUT was repeated 3 times and averaged.

For the OSDI questionnaire, the total points were multiplied by 25 and then divided by the total number of responses. To study the severity of symptoms, OSDI scores were grouped as normal (0–12), mild (13–22), moderate (23–32), and severe (≥33) as described previously in other studies.

All tear function tests were conducted in a quiet room of relatively constant temperature and humidity. The same experienced observer performed all measurements.

All surgeries were performed by one surgeon (M.G.) using Technolas 217 z100 excimer laser system (Bausch & Lomb, Rochester, NY). After topical anesthesia (Tetracaine 0.5%), an eyelid speculum was inserted. The amount of ablation performed was based on cycloplegic refraction and the patients’ age. Mitomycin C (MMC) 0.02% was applied to the stromal bed for up to 60 s. The surface was irrigated with a balanced salt solution. After PRK, topical antibiotics were instilled, and a bandage contact lens (Acuvue; Johnson & Johnson Vision Care, Jacksonville, FL) was applied.

All tear function tests were performed at least 5 days before surgery and also we followed the same postoperative eye drop protocol in all eyes. Postoperative treatment included Ciprofloxacin eye drops 4 times and Betamethasone 0.1% eye drops 6 times daily. On day 6 of follow-up, patients were assessed for complete corneal epithelial healing and consequently, contact lenses were removed. Up to 1 month after surgery, Fluorometholone and lubricant eye drops were used 4 times daily, and then Fluorometholone was tapered slowly the following 4 weeks.

Postoperative follow-up evaluation was scheduled 3 months after surgery. A complete ophthalmic examination including visual, refractive, and tear film function assessment was done. The main outcome measures of interest were the Schirmer and TBUT tests as clinical markers for tear film function and OSDI questionnaire as a subjective indicator of patients’ experience of dry eye symptoms, with a comparison of these parameters between the two groups.

Statistical analysis

We performed statistical analysis using SPSS software version 20.0 for Windows (SPSS, Chicago, IL, USA). The Chi-square test was used to compare the differences between Normal and Low STV groups. The pre- and post-operative values were compared for each group by paired t test. Pearson's correlation test was used to assess the relationship between the studied parameters. Results were explained as mean ± SD. p < 0.05 was considered statistically significant.
Results

Preoperatively, there were no significant differences between the two groups in age, gender, spherical equivalent (SE) refraction, and visual acuity (Table 1).

Preoperatively, the mean Schirmer test values were 8.36 ± 1.87 mm and 29.0 ± 6.78 mm in the low and normal STV groups, respectively (p < 0.001). It decreased to 6.17 ± 2.44 mm and 24.97 ± 9.21 mm 3 months after surgery (Fig. 1). The change in the two groups was statistically significant (both p < 0.001), but the change in tear secretion was significantly greater in the low STV group (p = 0.012).

The mean TBUT scores were 11.17 ± 2.51 s and 18.32 ± 4.57 s before, and 9.03 ± 1.96 s and 13.77 ± 5.36 s 3 months after surgery in the low and normal STV groups, respectively (p < 0.001) (Fig. 2). The decrease in TBUT scores was statistically significant in both groups (both p < 0.001). The change was greater in the normal STV group (p = 0.021) (Table 2).

The mean preoperative OSDI scores were 13.46 ± 7.11 and 14.52 ± 8.10 (p = 0.668) which changed to 16.23 ± 10.58 and 16.00 ± 10.15 at 3 months in the low and normal STV groups, respectively (p = 0.947) (Fig. 3). There were no significant differences between the two groups of participants for their OSDI scores and between pre- and postoperative scores in each group.

Correlation between TBUT and Schirmer values were significant (p < 0.001), but there was no significant correlation between OSDI score with TBUT (p = 0.803) and Schirmer values (p = 0.864).

Discussion

Dry eye is the most common postoperative complication in the vast majority of patients who undergo photorefractive procedures. It is also found that dry eye may enhance the corneal haze after PRK. A normal tear film layer plays a significant role in the ocular comfort and patient's satisfaction of operation and is important in the healing of the stroma and epithelium. Therefore, tear function assessment is essential before any corneal ablation.

There is still no gold standard model for evaluating tear film function and determining dry eye severity. Tear

Table 1
Demographic data of the subjects included in this study.

|                      | Low STV | Normal STV | p Value |
|----------------------|---------|------------|---------|
| Age                  | 26.19 ± 3.79 | 27.82 ± 3.42 | 0.053   |
| Gender, female/male  | 26/14   | 20/16      | 0.408   |
| Preoperative SE, D   | −3.56 ± 1.23 | −3.17 ± 1.17 | 0.156   |
| Preoperative Mar UDV A | (−1.25 to −6.00) | (−1.25 to −5.25) |         |
| Preoperative Mean log | 0.95 ± 0.39 | 1.00 ± 0.38 | 0.435   |
| Preoperative Mar CDVA | (0.2−1.3)   | (0.15−1.3)  |         |
| Preoperative Mean log Mar CDVA | 0.06 ± 0.09 | 0.04 ± 0.05 | 0.362   |

SE, spherical equivalent; UDV A, uncorrected distance visual acuity; CDVA, corrected uncorrected distance visual acuity.
function status is typically assessed using clinical signs or symptom-based questionnaires. A number of questionnaires have been developed and employed in both epidemiological studies and clinical research. Among the symptom questionnaires available, OSDI is one of the most widely used questionnaires. Objective markers can be measured with the tear and corneal function tests, consisting of Schirmer test to assess tear secretion (basal and reflex), TBUT to assess tear film stability, and Rose Bengal and corneal fluorescein dye staining to assess corneal epithelial integrity, tear film osmolarity, lysozyme, and lactoferrin assays.

Although tear osmolarity measurement is currently the most sensitive and specific diagnostic test for dry eye, the Schirmer test, despite its inaccuracy, remains the mainstay among these investigations in the clinical diagnosis of dry eye because of ease and better availability.

In this study, we investigated tear secretion, tear film stability, and dry eye symptoms after PRK and compared their values between eyes with preoperative low and normal Schirmer test values. We tried to improve the accuracy of the Schirmer test by performing the test with topical anesthesia (Schirmer 2), eye closure, and proper position of the strips as suggested by Holly et al.

A reduction in Schirmer values was observed for both normal and low STV groups 3 months after surgery. However, deterioration in tear secretion was significantly greater in the low STV group (p = 0.012). Based on these findings, we expected severity of symptoms to be higher in the low STV group postoperatively, as previous studies demonstrated patients with preoperative dry eye exhibited more severe symptoms and ocular surface damage after photorefractive surgery compared with non-preexisting dry eye patients. Based on our study, however, 3 months after surgery, no differences in subjective patient experience of dry eye symptoms between patients with preoperative normal and low Schirmer test values as demonstrated by results of OSDI were noted. Moreover, the differences between pre- and post-operative OSDI scores were not significant in either group. These findings conflicted with some previous comparative studies. Additionally, although the decrease in TBUT scores was statistically significant in both groups, tear film stability was more compromised in the normal STV group (p = 0.021).

At present, we do not have a clear explanation for these findings. It is difficult to understand the impact of tear film dysfunction on a patient, as many patients that show early clinical signs of dry eye disease may be asymptomatic, while others may report symptoms greater than their clinical signs. Based on clinical findings of previous studies, no consistent relationship and correlation exist between any of the common signs and symptoms of dry eye and between commonly used clinical tests.

However, previous studies have also revealed that the severity of dry eye affect on range of observed values of each sign, and patients with mild/moderate dry eye have a dynamic range of test values. Therefore, the correlation between sign and symptoms is probably stronger in eyes with severe dry eye. This indicates that although preoperative tear function plays an important role in postoperative tear secretion and stability, in eyes with preoperative mild dry eye, it may not lead to more symptoms after surgery.

Moreover, in this study, there was not a significant correlation between Schirmer test and OSDI. Previous studies have found that the Schirmer test may not be a good indicator for symptoms. The reason may be poor repeatability of Schirmer test. Also, the decrease in Schirmer values may not be enough to induce the symptoms.

Clinical signs alone seem insufficient to delineate those who have dry eye and those who do not, especially in the early stages of tear film dysfunction. A positive diagnosis of dry eye is often based heavily on the presence of symptoms, with literature suggesting that symptoms are an essential component of the disease.

This study had some limitations including performing only two clinical indicators of dry eye (Schirmer and TBUT) tests and a follow-up period of 3 months. A more comprehensive combination of assessments would provide a more accurate diagnosis of dry eye status. This would include a measure of tear osmolarity, corneal sensitivity, TBUT, Schirmer test, and corneal staining tests.

In conclusion, this study demonstrated decreased tear secretion after PRK. The authors suggest that patients who receive PRK should be informed of this risk, especially those with preoperative borderline tear secretion. However, any
refractive surgery candidate with signs or symptoms of dry eye should be stringently evaluated preoperatively. Additionally, proper management for tear function are required following surgery to eliminate complications.

References

1. Lee JB, Ryu CH, Kim J, Kim EK, Kim HB. Comparison of tear secretion and tear film instability after photorefractive keratectomy and laser in situ keratomileusis. J Cataract Refract Surg. 2000;26:1326–1331.
2. Paiva CS, Chen Z, Koch DD, et al. The incidence and risk factors for developing dry eye after myopic LASIK. Am J Ophthalmol. 2006;141:438–445.
3. Netto MV, Mohan RR, Ambrósio Jr R, Hutcheon AEK, Zieske JD, Wilson SE. Wound healing in the cornea: a review of refractive surgery complications and new prospects for therapy. Cornea. 2005;24:509–522.
4. Denoyer E, Landman L, Trinh J, Faure F, Aucin C. Dry eye disease after refractive surgery: comparative outcomes of small incision lenticule extraction versus LASIK. Ophthalmology. 2015;122:669–676.
5. Garcia-Zalisnak D, Nash D, Yeu E. Ocular surface diseases and corneal refractive surgery. Curr Opin Ophthalmol. 2014;25:264–269.
6. Raaoof D, Pineda R. Dry eye after laser in-situ keratomileusis. Semin Ophthalmol. 2014;29:358–362.
7. Torricelli AAM, Bechara SJ, Wilson SE. Screening of refractive surgery candidates for LASIK and PRK. Cornea. 2014;33:1051–1055.
8. Jabbar NS, Sakatani K, O’Brien TP. Survey of complications and recommendations for management in dissatisfied patients seeking a consultation after refractive surgery. J Cataract Refract Surg. 2004;30:1867–1874.
9. Levinson BA, Rapuano CJ, Cohen EJ, Hammersmith KM, Ayres BD, Laibson PR. Referrals to the Wills Eye Institute Cornea Service after laser in situ keratomileusis: reasons for patient dissatisfaction. J Cataract Refract Surg. 2008;34:32–39.
10. Levit AET, Galor A. Weiss JS, et al. Chronic dry eye symptoms after LASIK: parallels and lessons to be learned from other persistent postoperative pain disorders. Mol Pain. 2015;11:120–125.
11. Abetz L, Rajagopalan K, Mertzianis P, et al. Development and validation of the impact of dry eye on everyday life (IDEEL) questionnaire, a patient-reported outcomes (PRO) measure for the assessment of the burden of dry eye on patients. Health Qual Life Outcomes. 2011;9:111.
12. Brewitt H, Sistani F. Dry eye disease: the scale of the problem. Surv Ophthalmol. 2001;45:199–202.
13. Grubbs JR, Tolleson-Rinehart S, Huykh N, Davis RM. A review of quality of life measures in dry eye questionnaires. Cornea. 2014;33:215–218.
14. Behrens A, Doyle JJ, Stern L. Dysfunctional tear syndrome: a Delphi approach to treatment recommendations. Cornea. 2006;25:900–907.
15. Berry S, Mangione CM, Lindblad AS, McDonnell PJ. Development of the national eye institute refractive error correction quality of life questionnaire: focus groups. Ophthalmology. 2003;110:2285–2291.
16. Nettune GR, Pflogfelder SC. Post-LASIK tear dysfunction and dysesthesia. Ocul Surf. 2010;8:135–145.
17. Ambrosio RJ, Tervo T, Wilson SE. LASIK-associated dry eye and neurotrophic epitheliopathy: pathophysiology and strategies for prevention and treatment. J Refract Surg. 2008;24:396–407.
18. Seiler T, Wollensak J. Myopic photorefractive keratectomy with the excimer laser: one-year follow-up. Ophthalmology. 1991;98:1156–1163.
19. Konome K, Chen LL, Tarko RS. Preoperative characteristics and a potential mechanism of chronic dry eye after LASIK. Invest Ophthalmol Vis Sci. 2008;49:168–174.
20. Albietz JM, Lenton LM, McLennan SG. Dry eye after LASIK: comparison of outcomes for Asian and Caucasian eyes. Clin Exp Optom. 2005;88:89–96.
21. Albietz JM, Lenton LM. Management of the ocular surface and tear film before, during, and after laser in situ keratomileusis. J Refract Surg. 2004;20:62–71.
22. Yu EY, Leung A, Rao S, Lam DS. Effect of laser in situ keratomileusis on tear stability. Ophthalmology. 2000;107:2131–2135.
23. Ang R, Dartt D. Dry eye after refractive surgery. Curr Opin Ophthalmol. 2001;12:318–322.
24. Toda I, Asano-Kato N, Hori-Komai Y, Tsubota K. Laser-assisted in situ keratomileusis for patients with dry eye. Arch Ophthalmol. 2002;120:1024–1028.
25. Toda I, Asano-Kato N, Hori-Komai Y. Ocular surface treatment before laser in situ keratomileusis in patients with severe dry eye. J Refract Surg. 2004;20:270–275.
26. Schiffman RM, Christianson MD, Jacobsen G, Hirsch JD, Reis BL. Reliability and validity of ocular surface disease index. Arch Ophthalmol. 2000;118:615–621.
27. Miller KL, Walt JG, Mink DR. Minimal clinically important differences for the ocular surface disease index. Arch Ophthalmol. 2010;128:94–101.
28. Dougherty PJ, Wells BH, Maloney RK. Excimer laser ablation rate and corneal hydration. Am J Ophthalmol. 1994;118:169–176.
29. Tuft SJ, Galtry DS, Rawe IM, Meek KM. Photorefractive keratectomy: implications of corneal wound healing. Br J Ophthalmol. 1993;77:243–247.
30. Sullivan BD, Whitmer D, Nichols KK. An objective approach to dry eye disease severity. Invest Ophthalmol Vis Sci. 2010;51:6125–6130.
31. Schein OD, Tielsch JM, Munoz B. Relation between signs and symptoms of dry eye in the elderly. Ophthalmology. 1997;104:1395–1401.
32. 2007 Ethos Communications, Inc. Methodologies to diagnose and monitor dry eye disease: report of the Diagnostic Methodology Subcommittee of the International Dry Eye Workshop. Ocul Surf. 2007;5:108–152.
33. Ozcura F, Aydin S, Helvaci MR. Ocular surface disease index for the diagnosis of dry eye syndrome. Ocul Immunol Inflamm. 2007;15:389–393.
34. Vitale S, Goodman LA, Reed GF, Smith JA. Comparison of the NEI-VFQ and OSDI questionnaires in patients with Sjogren's syndrome-related dry eye. Health Qual Life Outcomes. 2004;2:44.
35. Dohlman Thomas H, Lai Edward C, Ciralsky Jessica B. Dry eye disease after refractive surgery. Int Ophthalmol Clin. 2016;56:102–111.
36. Lamberts DW. Physiology of the tear film. In: Smolin G, Thoft RA, eds. The Cornea. Scientific Foundations and Clinical Practice. 3rd ed. Boston MA: Little Brown; 1994:444.
37. Korb DR. Survey of preferred tests for diagnosis of the tear film and dry eye. Cornea. 2000;19:483–486.
38. Holly FJ. Lacrimation kinetics as determined by a Schirmer-type technique. Adv Exp Med Biol. 1994;350:543.
39. Lemp MA, Baudouin C, Amrane M. Poor correlation between dry eye disease (DED) signs and symptoms in a phase III randomized clinical trial. Invest Ophthalmol Vis Sci. 2011;52:3821.
40. Begley CG, Chalmers RL, Abetz L. The relationship between habitual patient-reported symptoms and clinical signs among patients with dry eye of varying severity. Invest Ophthalmol Vis Sci. 2003;44:4753–4761.
41. Nicholas KK, Nicholas JJ, Mitchell GL. The lack of association between signs and symptoms in patients with dry eye disease. Cornea. 2004;23:762–770.
42. Sullivan BD, Crews LA, Messmer EM, et al. Correlations between commonly used objective signs and symptoms for the diagnosis of dry eye disease. Clinical implications. Acta Ophthalmol. 2014;92:161–166.
43. Nelson JD, Farris RL, Sonmez B. Clinical utility of objective tests for dry eye disease (DED) signs and symptoms in patients with keratoconjunctivitis sicca. Arch Ophthalmol. 1988;106:484–487.
44. Sullivan BD, Crews LA, Sonmez B. Clinical utility of objective tests for dry eye disease: variability over time and implications for clinical trials. Cornea. 2012;31:1000–1008.
45. P1 Cho, Yap M. Schirmer test. II. A clinical study of its repeatability. Optom Vis Sci. 1993 Feb;70:157–159.