

Utility of Prosthetic Replacement of the Ocular Surface Ecosystem Treatment in the Management of Patients with Refractory Intrinsic Evaporative Dry Eye Disease

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Abstract

Background: Dry eye disease is a multifactorial disease whose pathogenic mechanisms have not been investigated rigorously. The objective of this study was to evaluate the utility of Prosthetic Replacement of the Ocular Surface Ecosystem (PROSE) treatment in the management of patients with intrinsic evaporative dry eye refractory to conventional therapies.

Design: A retrospective clinical cohort study of patients with intrinsic evaporative dry eye disease refractory to conventional therapies seen between July 1, 2009 and May 31, 2012 at USC Eye Institute, a tertiary referral center.

Participants: 36 eyes of 21 patients with intrinsic evaporative dry eye that completed PROSE fitting were included.

Main outcomes measures: Outcomes based on pre and post PROSE visual acuity and visual function. Best-corrected visual acuities were measured using a Snellen chart under standardized conditions. Visual function was assessed using the Ocular Surface Disease Index survey, a 12-item questionnaire that quantifies the severity of ocular discomfort and level of vision-related function.

Results: Mean visual acuity improved from 0.33 ± 0.40 logMAR pre-PROSE to 0.10 ± 0.16 logMAR post-PROSE ($Z=-4.3$, $p<0.0001$, $n=36$). Thirteen of 21 patients completed pre-PROSE and post-PROSE surveys. Survey scores improved from 63.61 ± 15.76 pre-PROSE to 24.84 ± 29.58 post-PROSE ($Z=-2.9$, $p=0.004$, $n=13$).

Conclusion: The results of our study strongly suggest PROSE treatment improves visual acuity and function in patients with refractory intrinsic evaporative dry eye disease and could serve as a viable alternative to more invasive procedures.

Keywords: PROSE; Dry Eye Disease

Introduction

Dry eye disease is a multifactorial disease that results from a complex interaction between environmental and patient-specific factors, and leads to symptoms of redness, pain, and loss of vision [1]. It is one of the most common causes of visual impairment in the U.S, with approximately 25% of the population reporting symptoms secondary to an abnormal ocular surface [1]. Examples of environmental factors that contribute to dry eye disease include entities that promote tear evaporation such as low humidity and wind. Patient-specific factors were broadly categorized by the 2007 Dry Eye Workshop Definition and Classification Subcommittee into either "aqueous deficient" causes that result in decreased tear production or "evaporative" causes that result in increased tear evaporation [2]. Examples of decreased tear production include Sjogren syndrome, lacrimal gland dysfunction, lacrimal gland duct obstruction, and reflex hyposecretion. Patient-specific causes of increased tear evaporation are further subdivided into intrinsic causes, including meibomian gland

dysfunction, low blink rate, and disorders of lid aperture, and extrinsic causes, such as contact lens wear, toxic keratitis, Vitamin A deficiency, and other ocular surface diseases such as cicatrizing conjunctivitis. The diagnosis of dry eye disease is made from a combination of patient's symptoms, clinical examination and ancillary testing such as tear-breakup time and tear secretion measurements. In light of the multifactorial nature of dry eye disease, it is not surprising that its prevalence is high and patients frequently suffer from pain, irritation, decreased vision, and decreased quality of life [3].

For many patients with dry eye disease, conventional treatments, such as artificial tears, soft contact lenses, and oral supplements, can provide symptomatic relief, but there is a subgroup of patients who are refractory to conventional treatments. Furthermore, differences in assessment of dry eye disease severity and treatment responses between patients and clinicians indicate that clinicians are more likely to underestimate disease severity and treatment efficacy, suggesting that the burden of morbidity for dry eye patients may be higher than current estimates [4].

The Prosthetic Replacement of the Ocular Surface Ecosystem (PROSE) treatment (Boston Foundation for Sight, Needham, MA) utilizes proprietary fitting software to custom design a large diameter scleral lens that vaults the entire cornea and limbus. The diameter of the device used in PROSE treatment ranges from 17.0 mm to 23.0 mm, and allows for a fluid reservoir to be filled with non-preserved sterile saline. The proprietary software used in PROSE treatment allows for customization to the individual patient's eye for maximum visual improvement and comfort [5]. Several studies have shown that scleral contact lenses significantly improve visual acuity and function in patients with various ocular surface diseases, including Stevens-Johnson syndrome, keratoconjunctivitis sicca, and chronic ocular graft vs. host disease [6-11]. PROSE treatment has been shown to significantly improve visual acuity and function in patients with conditions such as irregular corneal shapes, Salzmann's nodular degeneration, Stevens-Johnson syndrome, and thermal injuries to the ocular surface [6,12-16].

Due to the relatively novel nature of PROSE treatment, there is a paucity of studies investigating its efficacy in dry eye patients [17]. Conventional contact lenses are known to exacerbate dry eye symptoms in many dry eye patients [18]. We hypothesized that the innovative design of the device used in PROSE treatment would provide improvements in visual acuity and function for patients with dry eye disease. Given the enormity of dry eye etiologies, this report focuses on a cohort of patients with intrinsic evaporative dry eye disease. The purpose of this study was to evaluate the utility of PROSE treatment in management of intrinsic evaporative dry eye patients who had failed conventional therapies with outcomes based on visual acuity and function.

Methods

Patients

This retrospective chart review study was carried out in accordance with The Code of Ethics of the World Medical Association for experiments involving human subjects, and was approved by the University of Southern California Institutional Review Board. A preliminary review of charts from July 1, 2009 to May 31, 2012 identified 134 individuals with dry eye disease who were not satisfied with their existing treatment regimen and were referred to USC Eye Institute for PROSE treatment consultation. Patients with intrinsic evaporative dry eye disease, defined as meibomian gland dysfunction, disorders of the lid aperture, or low blink rate, were identified and included. Patients with other causes of dry eye disease such as Sjogren syndrome, graft versus host disease, Stevens-Johnson syndrome, and those who did not complete PROSE fitting were excluded. Ultimately, 36 eyes of 21 patients with intrinsic evaporative dry eye disease were identified and included in the study. All of the patients who met the inclusion criteria for the study were able to complete the PROSE fitting process. Demographic and clinical data including age, gender, number of visits required for the fit completion, ocular examination findings, and medications were recorded anonymously.

Device use

The patients included in our study were instructed to use PROSE throughout the day, removing it at bedtime. The fitting process included instruction on PROSE application and removal which differs from insertion and removal of traditional contact lenses due to its larger size, application of fluid within the reservoir, and use of an

applicator. Patients were also instructed on how to clean PROSE from mucus and debris that might accumulate throughout the day. The patients were asked during the post-PROSE survey if they wore their devices during waking hours all (100%), most (~75%), half (~50%), some (~25%), or none (0%) of the time.

Visual acuity

Visual acuity (VA) was recorded before and after PROSE fitting using a Snellen chart. Pre-PROSE VA was obtained using either manifest refraction or the patient's device at the time of initial evaluation for PROSE treatment. Post-PROSE VA was obtained at completion of the PROSE fitting. All visual acuities were obtained under standardized illumination with the projected image calibrated for the length of the examination room. Snellen acuities were converted to logarithm of the minimal angle of resolution (logMAR) acuities for statistical analysis [19].

Visual function

Visual function, pre and post PROSE fitting, was assessed using the Ocular Surface Disease Index (OSDI) survey [20]. This survey is a validated 12-item questionnaire designed to grade severity of ocular discomfort and vision-related function. OSDI scores range from 0 to 100, with higher scores representing greater functional disability. Pre-PROSE OSDI scores were obtained from the patient at the initial evaluation for PROSE treatment. For the purposes of this study, post-PROSE OSDI scores were obtained several months after the last fitting visit via telephone by a trained interviewer not involved in patient care. As the OSDI assesses overall ocular symptoms and function, patients receive a single score regardless of whether both eyes and a single eye underwent treatment.

Statistical analysis

Non-parametric statistical analysis was performed using Wilcoxon signed-rank test to compare pre and post PROSE visual acuities and OSDI scores.

Results

The study cohort included 36 eyes of 21 individuals with intrinsic evaporative dry eye disease who were refractory to conventional dry eye treatments and were managed with PROSE treatment. These patients were referred to the USC Eye Institute for PROSE evaluation by outside ophthalmologists after having exhausted therapies at their disposal. There were 9 males (43%) and 12 females (57%), and the mean age of the cohort was 56.3 years, ranging from 25 to 82 years. 15 patients (71%) were fitted with PROSE devices for both eyes, while 6 (29%) were fitted for one eye. 19 patients (90%) were White and 2 (10%) were Hispanic. By patient report, 16 of the 21 patients (76%) were using lubricating eye drops, 8 (38%) were using cyclosporine eye drops, 8 (38%) were using topical antibiotics, and 1 (5%) was using an oral antibiotic (doxycycline). 15 patients (71%) had previously received punctal plugs, 4 (19%) had been treated with autologous serum, and 2 (10%) had been treated with soft bandage contact lenses. All patients reported insufficient relief from their therapy regimen at the time of initial consultation. A mean of 4.5 visits, with a range of 3-8 visits, were required to complete PROSE fitting.

At initial presentation, all eyes showed meibomian gland dysfunction. 19 eyes (53%) had visible debris or mucus in the tear film,

and a reduced Tear Break-up Time (TBUT) less than 10 seconds was recorded in 12 eyes (33%). 2 eyes (6%) also showed lagophthalmos. Fluorescein staining showed varying degrees of punctate epithelial erosions (PEE) in 28 of 36 eyes (78%), ranging from rare to confluent PEE.

The mean pre-PROSE visual acuity (VA) in our cohort was 0.33 ± 0.40 logarithm of the minimal angle of resolution (logMAR), which correlates to a Snellen acuity of 20/45, and the mean post-PROSE VA improved to 0.10 ± 0.16 logMAR, which correlates to a Snellen acuity of 20/25, $Z=-4.3$, $p<0.0001$, $n=36$ (Figure 1A). A scatter plot of the data showed that 25 of 36 eyes (69%) had an improvement in VA following PROSE fitting, 11 of 36 eyes (31%) had the same VA pre and post PROSE fitting, and no eyes had worsening of VA following PROSE fitting (Figure 2A).

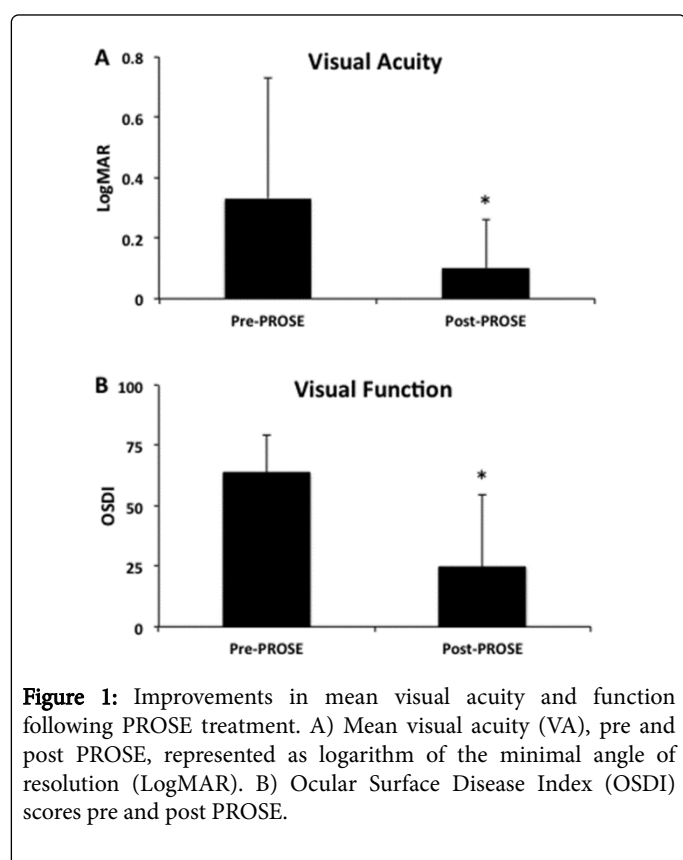


Figure 1: Improvements in mean visual acuity and function following PROSE treatment. A) Mean visual acuity (VA), pre and post PROSE, represented as logarithm of the minimal angle of resolution (LogMAR). B) Ocular Surface Disease Index (OSDI) scores pre and post PROSE.

Of the 21 patients, 1 (5%) declined to complete a pre-PROSE OSDI survey, and 7 (33%) declined or were unable to be reached for a post-PROSE OSDI survey due to relocation or death. The remaining 13 patients completed both the pre-PROSE and post-PROSE OSDI surveys. The post-survey was conducted on average 21 ± 13 months after the last fitting. At the time of the post-PROSE OSDI survey, 10 of the respondents (77%) reported using PROSE all or most of the time, 1 (8%) used PROSE half of the time, and 2 (15%) did not use PROSE at all. Those patients who reported not using PROSE ascribed their discontinuation to difficulty with insertion of the lens or a feeling that it was not helpful. Among the 13 patients, mean pre-PROSE OSDI score was 63.61 ± 15.76 , and the mean post OSDI score was 24.84 ± 29.58 , $Z=-2.9$, $p=0.004$, $n=13$ (Figure 1B). A scatter plots of the data showed that 11 patients (85%) had an improvement in the OSDI scores following PROSE treatment while 2 (15%) patients had slightly worse OSDI scores after PROSE treatment than before (Figure 2B). Of the

two with worse OSDI scores after treatment, both were fit for a device in the right eye only, one had discontinued wear of the device and reported an increase in OSDI of 19.3 at follow-up, and the other continued wearing it all of the time and reported an increase in OSDI of 8.6. At the time of the post-PROSE OSDI survey, 10 of the respondents (77%) reported using PROSE during waking hours all or most of the time, 1 (8%) used PROSE half of the time, and 2 (15%) did not use PROSE at all.

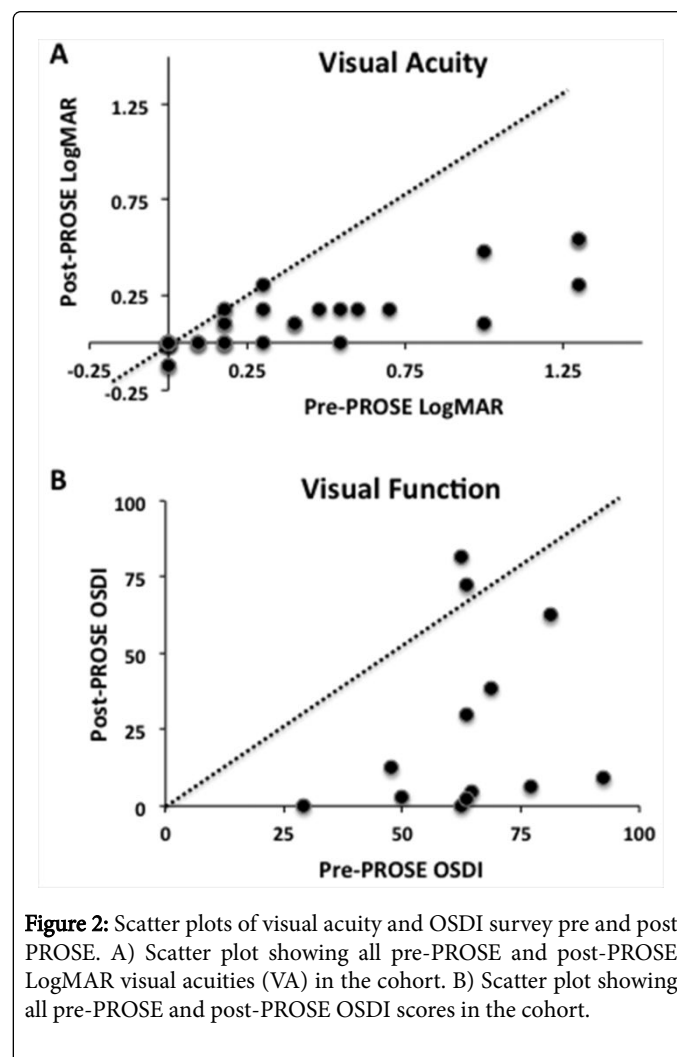


Figure 2: Scatter plots of visual acuity and OSDI survey pre and post PROSE. A) Scatter plot showing all pre-PROSE and post-PROSE LogMAR visual acuities (VA) in the cohort. B) Scatter plot showing all pre-PROSE and post-PROSE OSDI scores in the cohort.

Discussion

Poorly controlled dry eye disease can cause significant morbidity and detract from a patient's quality of life. This retrospective clinical cohort study suggests that PROSE treatment can significantly improve visual acuity and function in patients with intrinsic evaporative dry eye syndrome who had failed conventional therapies. The most common cause of intrinsic evaporative dry eye disease in our cohort was meibomian gland dysfunction. In our cohort, the mean visual acuity improvement was approximately four Snellen lines, and OSDI scores decreased in 11 of 13 patients who completed both initial and follow-up OSDI surveys. The mean OSDI score improvement of nearly 40 points, which correlates to a 60% regaining of symptoms and functions to normal, represents a marked improvement in these patients.

While recent studies have shown the efficacy of PROSE treatment for various ocular conditions, the effect on visual function and acuity in patients with intrinsic evaporative dry eye has not been reported. Dimit et al. showed clinical value of PROSE treatment in a cohort of 25 patients with moderate to severe dry eye syndrome; however their cohort included dry eye patients with multiple underlying etiologies [15]. Changes in best-corrected visual acuity and Visual Function Questionnaire (VFQ) scores in their dry eye cohort trended toward but did not achieve statistical significance, suggesting that some forms of dry eye disease are more amenable to PROSE treatment than others. This is not surprising given the multifactorial etiology of dry eye disease. The etiology of dry eye disease in our cohort was narrower, and our patients shared several clinical features. All patients in our study presented with meibomian gland dysfunction and many had tear film debris or mucus at initial consultation. Most patients also showed varying degree of superficial punctate epithelial erosions. All had failed multiple conventional dry eye treatments such as topical lubrication, topical cyclosporine, and soft contact lenses. While our results indicate that PROSE treatment is beneficial for patients with intrinsic evaporative dry eye disease, it is not known whether other dry eye etiologies will show a similar beneficial treatment response. The results of Dimit et al. study suggest that some forms of dry eye disease will be refractory to PROSE treatment, and further studies are needed to delineate which etiologies of dry eye disease are amenable to PROSE treatment.

One of the strengths of our study was the use of follow-up OSDI surveys to assess visual function pre and post-PROSE fitting. The OSDI survey is a validated measurement tool for assessing vision-related limitations and ocular discomfort. The three subsets of questions query different aspects of a patient's ocular condition, including symptoms experienced, ocular-related functioning, and tolerance of various environmental triggers [18].

Our study had several limitations. The relatively high rate of success, 10 patients using PROSE all or most of the time, and low rate of failure, 1 using PROSE half the time and 2 not using PROSE at all, introduces an ascertainment bias because the study included only patients who were successfully treated with PROSE treatment and did not include patients who were not deemed appropriate candidates. The study also did not have a control group of refractory intrinsic evaporative dry eye patients who were randomized to another treatment to compare visual acuity and function, however a lack of effective therapies for these patients make addressing this limitation difficult. Additionally, the small size of the cohort precluded subgroup analysis to compare results by different etiologies of intrinsic evaporative dry eye. Due to the retrospective design of the study, the OSDI follow-up times varied between participants in the study, and eight patients were lost to follow-up before a post-treatment OSDI could be attained. In a larger cohort, this variability would have allowed for comparison of scores by time after treatment; however such analysis was limited in our sample. The cohort was also predominantly White; therefore it is not known whether our results can be extrapolated to other groups.

The results of our study indicate that patients with intrinsic evaporative dry eye who did not respond to conventional therapies showed improvements in visual acuity and function with PROSE treatment, and it can provide an alternative option for patients who may be considering more invasive options such as tarsorrhaphy or punctual cautery.

Acknowledgements

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