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Case report

Improvement of chronic corneal opacity in ocular surface disease with prosthetic replacement of the ocular surface ecosystem (PROSE) treatment

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ABSTRACT

Purpose: To demonstrate clearing of chronic corneal opacities and improvement of visual acuity with the use of BostonSight prosthetic replacement of the ocular surface ecosystem (PROSE) treatment in ocular surface disease.
Observations: We undertook retrospective analysis of the medical records of a series of patients who underwent PROSE treatment from August 2006 to December 2014. Patients were referred for ocular surface disease of various etiologies. Primary inclusion criterion was corneal opacity that improved with PROSE treatment. Patients were excluded if topical steroids or adjuvant therapy used once PROSE treatment was initiated. Underlying disease, prior treatment, clinical presentation, and clinical course were extracted from the medical record. Four patients are included in this series. There were three females and one male; median age at time of treatment initiation was 30 years (range = 0.5–58 years). Median duration of PROSE treatment at time of retrospective analysis was 3.5 years (range = 1–8 years). Two cases had corneal opacification in the context of neurotrophic keratopathy: a unilateral case due to presumed herpes simplex keratitis and a bilateral case due to congenital corneal anesthesia associated with familial dysautonomia. One case had corneal opacity from exposure related to seventh nerve palsy, and one had corneal opacification associated with recurrent surface breakdown, neurotrophic keratopathy, and limbal stem deficiency of uncertain etiology. After consistent wear of prosthetic devices used in PROSE treatment for support of the ocular surface, visual acuity improved and clearing of the opacities was observed, without use of topical steroids or adjuvant therapy.
Conclusions and importance: These cases demonstrate clearing of chronic corneal opacity with PROSE treatment for ocular surface disease. This clearing can occur with no adjuvant therapy, suggesting that restoration of ocular surface function and integrity allows for corneal remodeling.

1. Introduction

Corneal transparency is heavily dependent upon the highly complex and regular spatial order of the collagen fibrils within the stromal layer.[1–5] Transparency can become compromised when the cornea is exposed to infection, trauma, chronic inflammation or ulceration.[6,7] When any of these occur, a series of complex wound healing mechanisms ensue, in order to protect the cornea and its integrity.[1,8–11] After injury or insult, the stroma begins to remodel and becomes significantly different in structure and composition from that of the normal corneal stroma. One way is different, is that it lacks matrix order. This lack of matrix order in the remodeling stroma may contribute to opacity formation.[1,11]

Even when lack of matrix order in the remodeling stroma is believed to contribute to corneal opacity after injury or insult, animal studies have shown that over time (months to years), collagen fibril size become progressively more regular and the stromal fibrils also become more organized in arrangement,[12] which are believed to be contributing processes in the potential return of corneal transparency.[2,12]

Surgical intervention such as phototherapeutic keratectomy (PTK), lamellar keratoplasty, and penetrating keratoplasty (PK) are typically undertaken for chronic opacities that limit vision. Typically these are classified as “scars.” Surgical intervention has inherent risk of infection, and in the case of penetrating keratoplasty, bleeding and rejection. There are substantial resource requirements involved in post-operative care, including office visits and medications. While surgery may lead to anatomic success, contact lens rehabilitation or spectacle wear may nevertheless be required, with a time course for visual rehabilitation

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being as long as one year.[13]

PROSE treatment (developed by BostonSight, Needham, MA, www.bostonsight.org), uses FDA-approved custom designed prosthetic devices to support or replace impaired ocular surface system functions that protect and enable vision.[14]

While visual rehabilitation of corneal opacity with RGP contact lenses,[13] scleral lenses[14–19] and PROSE treatment[20–23] has been described, we believe that a role for therapeutic lenses for the clearing or resolution of chronic corneal opacity in the setting of ocular surface disease is not appreciated and has never been reported. We present a series of four cases of resolution of chronic corneal opacity and improvement of visual acuity with PROSE treatment.

2. Methods

This study was a retrospective interventional case series. This retrospective medical record review of patients with dry eye syndrome was deemed exempt from IRB review by New England Institutional Review Board, as under 10–125, for research involving the collection or study of existing data or records if the information is recorded by the investigator in such a manner that subjects cannot be identified.

We undertook retrospective analysis of the medical records of a series of patients who underwent PROSE treatment from August 2006 to December 2014. Patients were referred for dry eye syndrome of various etiologies. Primary inclusion criterion was corneal opacity that improved with PROSE treatment. Patients were excluded if topical steroids or any other topical and or surgical approach was used once PROSE treatment was initiated. Underlying disease, prior treatment, clinical presentation, and clinical course were extracted from the medical record.

PROSE treatment involves the design and custom fabrication of FDA-approved prosthetic devices for therapeutic use on a daily wear basis, made out of two high gas-permeable fluorosilicone-acrylate polymers (Dk 85 or 127×10^{-11}·cm^2 ·ml O_2/s ml mm Hg [ISO/Fatt]). All devices were designed and fabricated using a proprietary CAD/CAM technology to customize the bearing surface of the device haptic to align with the supporting sclera and a transitional and optic portion designed to vault the cornea. The device is filled with artificial tears at the time of application and removed for cleaning and disinfection. Assessment of physiological function with prosthetic devices used in PROSE treatment included evaluation of corneal clearance and haptic alignment, fluid ventilation, corneal status, and subjective tolerance after 1, 3–4, and 6–8 hours of prosthetic device wear. Routine photodocumentation of corneal findings using an RS-1000 Zoom Slit Lamp digital photo unit with a mounted Nikon D200 camera was an integral part of clinical assessment. Patients returned for evaluation of medical status and monitoring of device function at 1, 3 and 6 months after devices were dispensed and yearly after that.

3. Case report #1

An 11-year-old male was referred to BostonSight in November 2006 with an 18-month history of persistent epithelial defect (PED) in the left eye. Past ocular history was also significant for strabismic amblyopia in the left eye.

There was incidental report of tree branch injury to the left eye. He was referred with a presumptive diagnosis of herpes simplex neurotrophic keratitis. Previous treatments included two failed amniotic membrane grafts. His medications at time of referral included 400 mg oral acyclovir twice daily, autologous serum tears four times daily and sodium chloride hypertonic ointment nightly.

Entering uncorrected visual acuity at initial consultation was 20/20^+ in the right eye and 20/400 in the left eye, with improvement to 20/70 with pinhole (PH). On slit lamp examination, a central epithelial defect measuring 3 mm × 3.5 mm was noted (Fig. 1A), with 2 + central haze and 20–30% stromal thinning (Fig. 1B). Corneal sensitivity using a Luneau Cochet-Bonnet Aesthesiometer was measured at 0.5 cm in the right eye and 7 mm in the left eye. The remainder of the eye examination was unremarkable.

He was treated with a custom-fabricated device for the left eye that was worn overnight with prophylactic use of preserved-free moxifloxacin antibiotic and daily removal and disinfection as previously described.[18] The PED healed two weeks after initiating PROSE treatment. Best-corrected visual acuity once the PED healed improved to 20/70^{-2} PH 20/50^{-2}.

This patient was monitored over the next six years of daily wear of devices used in BostonSight PROSE treatment. No additional topical agents, such as corticosteroid or anti-viral agents were used, nor was any surgical intervention undertaken. There was no recurrence of surface breakdown or episode of epithelial of stromal keratitis. There was clearing of corneal opacity observed over the subsequent eight years of PROSE treatment (Fig. 2). Best corrected visual acuity in the left eye (with history of strabismic amblyopia) remained at 20/70 PH 20/50.

4. Case report #2

A 6-month old female was referred to BostonSight in September 2008. A diagnosis of congenital corneal anesthesia from Hereditary Sensory and Autonomic Neuropathy Type III, Familial Dysautonomia (once called Riley-Day syndrome) was made at three months of age. She had a history of superficial keratitis in both eyes and ulceration and persistent epithelial defects (PED) in the right eye that healed after three amniotic membrane grafts. At the time of the initial consultation visual function at the fixate and follow level could be confirmed for the left eye only.

Penlight and ophthalmoscope with blue light and Wratten #12 yellow filter examination showed corneal staining in the right eye more than left eye with no epithelial defects present at the time of consultation. There was corneal opacification with thinning in the right eye (Fig. 3A). A retinoscopic red reflex was obtained for the left eye but was undetectable in the right eye. PROSE treatment was undertaken for both eyes with power determination based on cycloplegic retinoscopy of the left eye.

At the visit three months later, her mother described improved visualization of right pupil (Fig. 2B). Fix and follow vision could be confirmed for left eye only.

She returned seven months later and a retinoscopic reflex could be obtained (Fig. 3B). Topical atropine had been prescribed back in September 2008 by her referring doctors for the right eye to aid in image formation around the opacity and discontinued eleven months after. Patching occlusion of the left eye for amblyopia treatment required upper extremity restraint and was abandoned. Eventually an occlusive soft contact lens was used over the device in her left eye for occlusion therapy.[19]

After 18 months of PROSE treatment, a decrease in the corneal opacity in the right eye was observed (Fig. 3C). Full cycloplegic refractive error, determined by retinoscopy, was prescribed for each prosthetic device. She could fixate, follow, and reach out for an object using each eye alone. Continued clearing of opacity and stability of the ocular surface was noted over the subsequent six years (Fig. 3D and E).

5. Case report #3

A 49-year-old female was referred to BostonSight in June 2013 with history of chronic exposure and superficial keratitis of the right eye associated with facial nerve palsy after head trauma at age 15. Previous treatments of the right eye included: partial tarsorrhaphy, upper lid weight, superior and inferior punctal occlusion, and nightly sodium chloride hypertonic ointment.

Entering corrected distance visual acuity was 20/50 + PH 20/30 in the right eye, 20/30 PH 20/15 in the left eye. Slit lamp evaluation revealed a partial tarsorrhaphy with incomplete blink, upper lid weight,