Accelerated Restoration of Ocular Surface Health in Dry Eye Disease by Self-Retained Cryopreserved Amniotic Membrane

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ABSTRACT **Purpose: To evaluate the clinical efficacy of self-retained cryopreserved amniotic membrane in treating dry eye disease. Methods: Retrospective review of 10 patients treated with self-retained cryopreserved amniotic membrane (PROKERA® Slim [PKS], Bio-Tissue, Miami, FL) for moderate-to-severe dry eye refractory to conventional maximal medical treatments. Patients' symptoms, use of medications, conjunctival inflammation, corneal staining, and visual acuity were compared before and after treatment. Results: PKS was placed in 15 eyes of the 10 patients for 4.9 ± 1.5 days. All patients experienced symptomatic relief for a period of 4.2 ± 4.7 months ($P<.001$). Such improvement was accompanied by reduction of OSDI scores ($P<.001$), use of topical medications ($P<.001$), conjunctival hyperemia ($P<.001$), corneal staining ($P<.001$), and improvement of the visual acuity ($P=.06$). Linear regression analysis estimated that the optimal duration of PKS placement was 5 days to achieve an average symptom-free duration of 4 months in patients with dry eye. Surprisingly, PKS placement also generated improvement in the contralateral eyes. Conclusion: This pilot study suggests that self-retained cryopreserved amniotic membrane via PKS can be used to treat moderate dry eye diseases and warrants further prospective controlled studies.**

KEY WORDS **amniotic membrane, dry eye, keratitis, ocular surface, PROKERA®**

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I. INTRODUCTION

Dry eye disease (**DED**) is a multifactorial disease of the tears and the ocular surface that results in discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface.[1] Progress has been made in the understanding of the etiology and pathogenesis of DED as well as other ocular surface diseases that mimic or aggravate DED. These advances have led us to adopt a practical algorithm for clinicians to restore the integrity of the ocular surface with an attempt to maintain a stable tear film.[2]

Despite different underlying pathogenic processes, DED is characterized by a common denominator of ocular surface inflammation. This, in turn, causes cell damage and a self-perpetuating cycle of deterioration. Therefore, interruption of this inflammatory cascade is a key tactic in preventing potential corneal surface damage and scarring.[2-4] Different treatment modalities have been tried to suppress inflammation, prevent further damage, and restore ocular surface integrity. These treatments include medications such as steroids and cyclosporine; however, results can be variable and refractory in some cases.

OUTLINE

Cryopreserved amniotic membrane (**CAM**) has anti-inflammatory, anti-scarring, and anti-angiogenic effects when transplanted to the ocular surface to treat different diseases.[5-7] CAM has been used as a temporary biological bandage by sutures or through a self-retaining device, (PROKERA® Slim [PKS], Bio-Tissue, Miami, FL, USA) to restore a healthy and smooth corneal epithelium in a variety of ocular surface diseases.[8] In this study, we retrospectively reviewed 10 consecutive cases of moderate-to-severe dry eye that had been treated by self-retaining CAM. Our preliminary results demonstrated its effectiveness in controlling inflammation, restoring ocular surface integrity, and reducing the frequency of concomitant topical medications.

II. METHODS

This study was approved by the ethics committee of the Ocular Surface Research and Education Foundation (Miami, FL) according to the Tenets of the Declaration of Helsinki to retrospectively review 10 patients (15 eyes) with moderate-to-severe DED that were consecutively seen at Ocular Surface Center (Miami, FL) between August 2013 and January 2015. Table 1 summarizes the patients' demographics, ocular comorbidity, previous therapies, clinical presentations, and concomitant medications at presentation. Patients completed an evaluation of the symptoms and signs of dry eye disease to be classified into the dry eye severity grade from 1 to 4, as published in the Report of the International Dry Eye Work Shop (**DEWS**) 2007.[1] The severity of symptoms was graded according to the Ocular Surface Disease Index (**OSDI**) score,[9] ranging from 0-12 (no disability), 13-22 (mild), 23-32 (moderate), and 33-100 (severe). Conjunctival inflammation was graded according to the conjunctival injection as none (0), mild (1), moderate (2), and severe (3). The corneal surface integrity was scored as clear (0), scattered superficial punctate keratitis (**SPK** [1]), moderate SPK (2), and diffuse SPK with or without corneal epithelial defects (3). Schirmer strip wetting by the fluorescein clearance test and tear film breakup time (**TFBUT**) were carried out as outlined in the DEWS report.[1] Concomitant medications and Snellen visual acuity were recorded.

Because of persistent symptoms and/or epithelial breakdown of the ocular surface despite maximal medical treatments, PKS was inserted in one eye at a given time with an attempt to alleviate the symptoms and restore the ocular surface health. After the patient's written consent was obtained, PKS was thawed at room temperature for a few minutes, rinsed with saline, and inserted in the office under topical anesthesia with 0.5% proparacaine hydrochloride eye drops. It was first placed into the superior fornix while the patient looked down and was then slid under the lower eyelid. After placement, the patients were asked to use or reduce the numbers of concomitant topical medications at will. Patients returned to the office for removal of the PKS and were followed up as needed thereafter. The followup visits were documented, and the patients were evaluated in the same manner as before the placement of PKS. These findings are also summarized in Table 1.

Descriptive statistics for continuous variables are reported as the mean ±SD and analyzed using SPSS software, version 19.0 (SPSS Inc, Chicago, IL, USA). Differences and correlation between parameters were analyzed by the student's t-test, the Wilcoxon signed ranks test, or the Spearman's rank order correlation. A P value less than .05 was considered statistically significant. A simple linear regression was calculated predicting PKS placement duration and symptom-free duration based on the symptoms severity and variables under investigation.

III. RESULTS

This study included 15 eyes of 10 patients (2 males and 8 females) with a mean age of 68.7 ± 16.2 years (range, 39 to 87 years). Relevant clinical data of each patient are summarized in Table 1. No associated systemic disease such as Sjögren disease, rheumatoid arthritis, systemic lupus erythematosus, progressive systemic sclerosis, polymyositis, or dermatomyosis that contributed to DED symptoms were reported among all patients. The 15 eyes had previously received 2.5 ± 0.9 (range, 1 to 5) topical concomitant medications, including autologous serum (10.8%, 4/37), artificial tears (48.6%, 18/37), steroid (21.6%, 8/37), cyclosporine (10.8%, 4/37), and antibiotics (8.1%, 3/37). Eleven out of 15 eyes (73%) received optimal conventional therapy, including bandage contact lens in 7 eyes (46.7%), punctal occlusion in 11 eyes (73%), and/or cauterization in 2 eyes (13%). Six out of 15 eyes (40%) underwent conjunctivochalasis (**CCh**) surgery (n=4), pterygium surgery (n=1), laser in situ keratomileusis (**LASIK**) (n=1), and blepharoplasty (n=1) with an average of 6 ± 3 (range, 1 to 10) years prior to PKS placement, whereas the mean duration of dry eye symptoms in the 15 eyes was 13.6 ± 11.8 (range, 1 to 37) years.

Despite the aforementioned medical treatments, the patients remained symptomatic and cited various complaints, including dryness (12/15 [80%]), irritation (12/15 [80%]), burning (5/15 [33.3%]), gritty sensation (9/15 [60%]), photophobia (8/15 [53.3%]), redness (7/15 [46.7%]), sharp pain (5/15 [33.3%]), soreness (5/15 [33.3%]), blurred vision (5/15 [33.3%]), itching (4/15 [26.7%]), sticky sensation (2/15 [13.3%]), and mucus formation (2/15 [13.3%]). The severity of symptoms was graded by the OSDI score as mild in 2 eyes (13.3%), moderate in 5 eyes (33.3%), and severe in 8 eyes (53.3%), with a mean score of 33.5 ± 10.8 (range, 18.8 to 54.2), indicating that our overall study population had moderate-to-severe dry eye symptoms. All eyes had corneal SPK with scoring as 1+ (mild) in 11 eyes (73.3%), 2+