ORIGINAL RESEARCH PAPER

Ophthalomology

ROLE OF FREEZE-DRIED AMNIOTIC MEMBRANE IN MANAGEMENT OF PERSISTENT EPITHELIAL DEFECT ON DRY EYE DISEASE

KEY WORDS:

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ABSTRACT

Purpose: To report the outcome of freeze-dried amniotic membrane for persistent epithelial defects (PED) in moderate to severe cases of dry eye disease. **Methodology:** This is retrospective-prospective observational study included consecutive patients of dry eye disease with persistent epithelial defects treated with freeze dried amniotic membrane and bandage contact lens. Included were patients with an epithelial defect that did not respond to conventional treatment. Excluded were the patients who failed to follow-up. **Results:** 30 eyes of 30 patients with mean age of 38.8 years (21-58 years) were included in this study. The main etiology of PED was superficial punctate keratitis (n=7/30), followed by chemical burns (n=4/30) and limbal stem cell deficiency (n=4/30), neurotrophic keratitis (n=3/30). Remaining cases were exposure keratitis, vernal keratitis, filamentary keratitis, GVHD, simple herpetic keratitis (n=2/30) respectively, Sjogren's syndrome (n=1/30), herpes zoster keratitis (n=1/30). Time from PED presentation to amnion treatment was 39.1 days (range 16-90 days). The amnion was absorbed within 2 weeks in 100% of the cases. Following insertion of the amnion, resolution of the PED was achieved in 26/30 eyes (86.6%) without the need for additional interventions within 20.7 days (range 7-35 days) with no complications recorded. **Conclusion:** Dried amniotic membrane achieved resolution of PEDs secondary to various etiologies of dry eye disease in 86.6% of eyes with a significant improvement in vision demonstrated. Further studies are needed to assess long term safety and effectiveness.

INTRODUCTION

The corneal epithelium serves as a protective barrier against infections and maintains a smooth optical surface.[1] If the epithelium is damaged, it can lead to corneal erosion, which increases the risk of infection and can impair vision. Normally, the epithelium undergoes a repair process that involves various factors such as growth regulation, cellular signalling, proliferation, migration, and remodelling of the extracellular matrix. However, when corneal epithelial defects persist for more than 10-14 days despite standard treatment, it is known as Persistent Corneal Epithelial Defects (PEDs). Possible causes of PEDs include faulty epithelialadhesion, deficiencies in limbal stem cells, inflammation, neurotrophic components, and idiopathic or hereditary disorders.[1]

The management of persistent corneal epithelial defects (PEDs) involves a step-by-step approach that depends on the underlying cause. Various non-surgical treatments are available, such as optimizing the ocular surface, using bandage contact lenses, employing blood-derived products like autologous serum and platelet-rich plasma, punctal plugs, scleral contact lenses, and cenegermin.[2] If non-surgical methods are not effective, surgical options can be considered, including epithelial debridement, amniotic membrane transplant (AMT), and corneal stem cell transplant.[4]

Amniotic membranes are known to contain numerous growth factors that facilitate wound healing, provide a scaffold for re-epithelialization, and possess anti-inflammatory properties.[5] As a result, they have been proven to be effective in the treatment of PEDs.[6,7] Commercially available amniotic membrane implantation such as the cryopreserved ProKera has shown promising results in treating bacterial keratitis,[8] alkali burns,[9] partial limbal stem cell deficiency,[10] acute toxic epidermal necrolysis,[11] and PEDs.[12] Freeze and vacuum dehydrated amnion tissue are also recently introduced, which can be easily stored and transported at room temperature.[13] This study is the first to evaluate the efficacy of sutureless dehydrated amniotic membrane treatment for PEDs in Western Rajasthan, India.

Methods

Source of data: - A hospital-based retrospective-prospective observational study (mixed design cohort study) to evaluate the role of freeze-dried amniotic membrane in reducing signs and symptoms of DED associated with ocular surface involvement. The study will be conducted for a period of five months from June 2022- November 2022 in the department of Ophthalmology, Dr. S. N Medical college, Mathura Das Mathur Hospital with due permission from the institutional Ethical Committee and Review Board after taking written informed consent from patient. The study included patients who did not experience sufficient resolution of the defect following ocular surface optimization and treatment with a BCL, as per the Global Consensus guidelines for managing Limbal Stem Cell Deficiency. This optimization process addressed any underlying comorbidities of the eyelid and conjunctiva, reduced toxicity from topical medications, lowered inflammation through various medications, improved tear function with preservative-free artificial tears and/or autologous serum, and treated underlying meibomian gland dysfunction. Patients with less than three months of follow-up were excluded from the study.

Data Collection: - Prior to surgery, demographic information such as gender, age, and laterality was recorded. Other baseline data collected included best-corrected visual acuity (BCVA), the cause of the persistent epithelial defect (PED), any systemic comorbidities, the size of the PED measured in square millimetres with fluorescein staining and cobalt flue filter, the duration between PED presentation and amnion treatment, the time it took for the PED to resolve after amnion treatment, follow-up time, and BCVA after resolution. Recurrences of the PED, any complications, or adverse events that occurred during the follow-up period were also documented.

Amniotic Membrane: - Amniocare-D, a dehydrated amniotic membrane that does not require sutures, was stored at room temperature before use. Patients were given proparacaine hydrochloride 0.5% eye drops and after five minutes, a lid speculum was inserted, and cellulose sponges were used to dry the cornea. In our experience, proper adhesion of the amniotic membrane to the corneal surface requires the corneal surface to be dry. A 9.0 mm circular amniotic membrane disc was placed over the centre of the cornea to cover the entire epithelial defect. However, care should be taken to prevent the amnion from folding on itself, which can

be achieved by using a second non-toothed curved forceps to smooth it onto the corneal surface immediately after placement. After 2 to 5 minutes, a sterile BCL was placed over the amnion and dried with cellulose eye sponges. Adequate positioning of the amnion and BCL was confirmed at the slit lamp 5 minutes later.

Patient Follow-up: - Patients were monitored every 1-3 weeks after the insertion of the amniotic membrane until the epithelial defect was resolved. During each visit, the area of the PED and BCVA were documented. If the PED showed adequate but incomplete resolution after the absorption of the amniotic membrane, the BCL treatment was continued.

Study Outcome: - The main objectives of the study were to assess the rate and duration of PED resolution, as well as any changes in BCVA and incidence of serious adverse events.

RESULTS

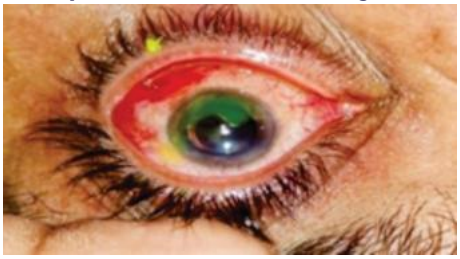
30 eyes of 30 patients with mean age of 38.8 years (range 21-58 years) were included in this study of which 23.33% (n=7) were of female gender and 76.67% (n=23) were males. The mean follow-up time of 45.66 days (range 21-89 days).

PED Etiologies: - The main etiology of PED was superficial punctate keratitis (n=7/30), followed by chemical burns (n=4/30) and limbal stem cell deficiency (n=4/30), neurotrophic keratitis (n=3/30). Remaining cases were exposure keratitis, vernal keratitis, filamentary keratitis, GVHD, simple herpetic keratitis (n=2/30) respectively, Sjogren's syndrome (n=1/30), herpes zoster keratitis (n=1/30).

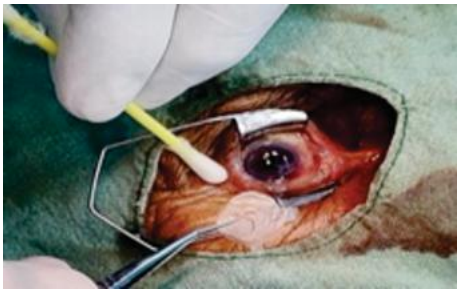
PED Duration: - Time from PED presentation to amnion treatment was 39.1 days (range 1690 days) with the area of the PED being 9.48 mm^2 (range 1-30 mm^2). The amnion was absorbed within 2 weeks in 100% of the cases. Following insertion of the amnion, resolution of the PED was achieved in 26/30 eyes (86.6%) without the need for additional interventions within 20.7 days (range 7-35 days) with no complications recorded.

Complications and Adverse Events: - No issues occurred during the amniotic membrane placement or during subsequent follow-up. None of the patients complained of any discomfort with the application of amnion and BCL on their ocular surface. There were no instances of PEDs recurring during the follow-up period.

Figure 1: - Dry Amniotic Graft With Bandage Contact Lens

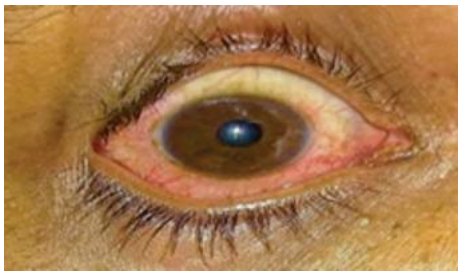


Pre Operative Image of PED



Intra Operative Image Before Dry AMG

Intra Op Image After AMG



Healed Epithelial Defect After 21 Days

DISCUSSION

This study is an observational analysis of the effects of dehydrated amniotic membrane transplantation on persistent epithelial defects (PEDs) in dry eye disease patients who have not responded to traditional treatments. In our study, we observed complete resolution of PEDs in 26 out of 30 eyes (86.66%) for various reasons, although incomplete recovery was observed in three cases, and one case of epithelial disorder in dry eye disease did not improve. The severity and persistence of multiple corneal erosions prevented complete healing in these cases. 73% of participants in our study showed significant improvement in corneal transparency, which is associated with improved visual acuity, emphasizing the healing properties of amniotic membrane grafts.

Previous studies on the effects of ProKera,[12] a type of amniotic membrane graft, have reported varying success rates and complications, including eye pain and headaches. The current study evaluated the use of dry amniotic membrane (Amniocare-D), a readily available amnion graft, for PEDs and reported an 86.66% resolution rate without any reports of pain or discomfort. The use of a bandage contact lens to secure the graft and the absence of a conformer ring may have improved patient comfort. The Amniocare-D was fully absorbed after a few weeks, which may make it a more appropriate option for monocular patients. The study also observed an improvement in best-corrected visual acuity postoperatively, likely due to the resolution of PEDs that involved the visual axis.

In a 2021 study by Michael Mimouni, Tanya Trinh, Nir Sorkin et al., BioDOPTIX amnion graft was used to treat patients with PED resulting from specific causes. After an average of 17.8 days, 89% of eyes achieved resolution of PEDs without any patient experiencing discomfort from the graft. There was also improvement in LogMAR BCVA from 0.94+ 0.88 to 0.37+0.25 (p=0.036). These findings were consistent with previous studies and our own study.

Another retrospective study by M McDonald et al. showed that self-retained CAM (cryopreserved amniotic membrane) can accelerate the recovery of corneal surface health in patients with mild and severe dry eye disease. A single placement of CAM for 5.4+2.8 days led to a significant improvement in DED symptoms and signs, with an overall significant reduction in DEWS scoring from 3.25+0.5 (baseline) to 1.44+0.6 at 1 week, 1.45+0.6 at 1 month, and 1.47+0.6 at three months. These findings were consistent with previous studies and our own study as well.

To sum up, the study demonstrates the efficacy of using dried amniotic membranes for treating different ocular surface disorders, especially persistent epithelial defects. The results indicate that dry amniotic membrane implantation is a safe, simple, convenient, and successful treatment for moderate to severe dry eye disease with multiple epithelial defects.

Declaration of Conflicting Interests: - The author declared no potential conflicts of interest with respect to the research, authorship, and/or publication of the article.

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