Outcomes of dried versus cryopreserved amniotic membranes on corneal epithelial defects

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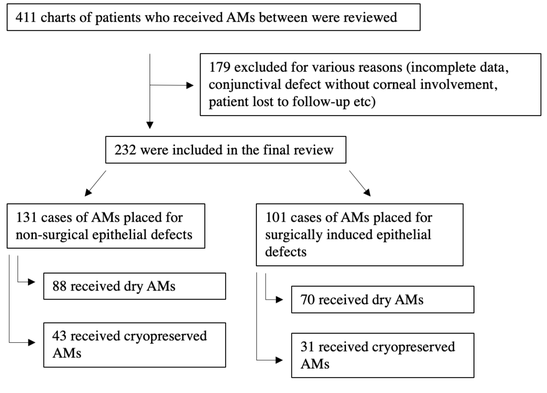
Background

The amniotic membrane (AM) is a collagenous membrane that is derived from the innermost layer of the placenta closest to the fetus.[1] It has been shown to promote epithelial wound healing and can serve as a scaffold for cell growth.[1-5] AMs can be processed into cryopreserved and dried forms.[1,5-6] The dried form is thought to contain lower amounts of the growth factors that contribute to its wound healing properties.[5-6] However, there is insufficient data on whether this translates to differences in clinical outcomes between cryopreserved and dried AMs. The aim of this study is to compare the outcomes of corneal epithelial defects after treatment with cryopreserved versus dried AMs.

Purpose and Methods

A retrospective chart review of patients who received AMs for corneal epithelial defects at Duke was performed. The type of AM, presenting best corrected visual acuity, indications for AM, and anterior segment exam were collected. Based on clinical documentation, patients were separated into epithelial defect fully healed, partially healed, no change, or worse groups. Subgroup analysis of surgically versus non-surgically induced epithelial defects was done. Statistical analysis was performed using R studio.

Figure 1: Study design



Results

Table 1: Overall results

Characteristic	Dry AM (n=158)	Cryopreserved AM (n=74)	P-value
Presenting logMAR, mean (SD)	1.30 (0.85)	1.24 (0.92)	0.70
Follow-up interval days, mean (SD)	10.75 (5.71)	12.49 (11.33)	0.21
Epithelium outcomes, No. (%)			
Healed	59 (37.3)	33 (44.6)	0.36
No change	24 (15.2)	12 (16.2)	0.99
Partially healed	60 (38.0)	22 (29.7)	0.28
Worse	15 (9.5)	7 (9.5)	1.0

Notes: P-values reflect comparison between dry and cryopreserved using 2-sided student's t tests and χ^2 comparisons where appropriate

Table 2: Surgically induced epithelium defect group results

Characteristic	Dry AM (n=70)	Cryopreserved AM (n=31)	P-value
Presenting logMAR, mean (SD)	1.11 (0.83)	1.22 (0.87)	0.57
Follow-up interval days, mean (SD)	10.22 (5.28)	10.29 (6.15)	0.96
Epithelium outcomes, No. (%)			
Healed	34 (48.6)	14 (45.2)	0.92
No change	9 (12.9)	7 (22.6)	0.35
Partially healed	20 (28.6)	8 (25.8)	0.96
Worse	7 (10.0)	2 (6.5)	0.84

Notes: P-values reflect comparison between dry and cryopreserved using 2-sided student's t tests and χ^2 comparisons where appropriate

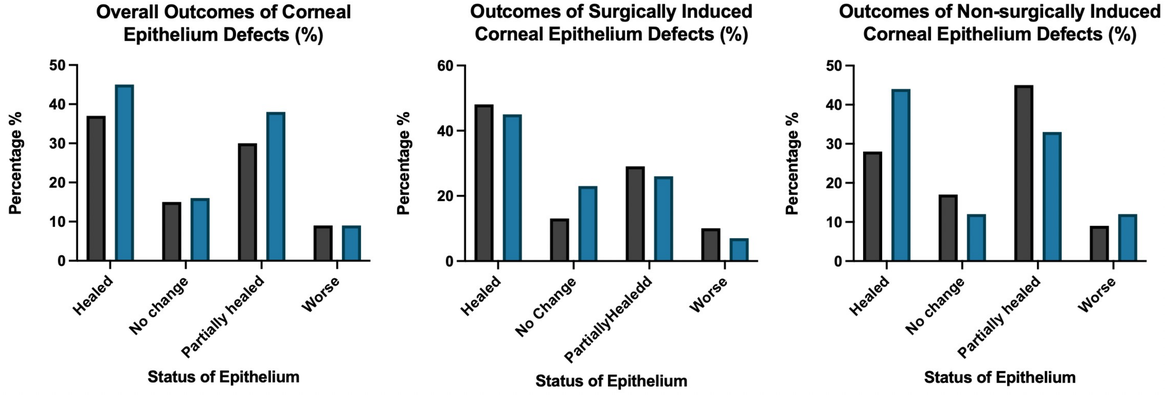
As shown in *Figure 1*, 411 charts of AM placements were reviewed and 232 involved corneal epithelial defects. Of these, 131 did not involve surgery and 101 were surgically induced. *Table 1* focuses on overall results. Patients treated with dried and cryopreserved AMs had similar presenting BCVA (1.30 vs 1.24 logMAR, p = 0.70). The dried and cryopreserved patients also had similar follow-up times after AM placement (10.75 vs 12.49 days, p=0.21). Epithelium outcomes for healed (37.3 vs 44.6 percent, p=0.36), partially healed (38.0 vs 29.7 percent, p=0.28), no change, (15.2 vs 16.2 percent, p=0.99) and worse (9.5 vs 9.5 percent, p=1) groups were not statistically significant between dried and cryopreserved AMs. Similarly, no significant results was found in the two subgroups (*Tables 2 and 3*).

Table 3: Non-surgically induced epithelium defect group results

Characteristic	Dry AM (n=88)	Cryopreserved AM (n=43)	P- value
Presenting logMAR, mean (SD)	1.44 (0.84)	1.26 (0.96)	0.31
Follow-up interval days, mean (SD)	11.16 (6.03)	14.07 (13.78)	0.19
Epithelium outcomes, No. (%)			
Healed	25 (28.4)	19 (44.2)	0.11
No change	15(17.0)	5 (11.6)	0.58
Partially healed	40 (45.4)	14 (32.6)	0.22
Worse	8 (9.1)	5 (11.6)	0.88

Notes: P-values reflect comparison between dry and cryopreserved using 2-sided student's t tests and χ^2 comparisons where appropriate

Figure 2: Corneal epithelial outcomes overall and for each subgroup



Conclusion

In this study, we have shown that dried and cryopreserved AMs resulted in similar outcomes when used to treat corneal epithelial defects. Cryopreserved AMs are stored frozen and must be thawed to room temperature before use while dried AMs have stable shelf lives of many years.[1,6] Our result is clinically important because these dried AMs can be much more easily utilized and accessed especially in resource limited circumstances.

Limitations and future directions

In this study, visual acuity was used as a proxy for overall eye health, and this was found to be not statistically significant between the two AM groups. However, this is only one parameter and more data collection of other variables representing eye health (such as number of prior surgeries, other ocular comorbidities, etc) could be done to make a better overall proxy for eye health and determine whether there are differences in AM use and outcomes depending on eye health.

References

1. Sabater AL, Perez VL. Amniotic membrane use for management of corneal limbal stem cell deficiency. Curr Opin Ophthalmol. 2017 Jul;28(4):363-369.
2. Grueterich M, Tseng SC. Human limbal progenitor cells expanded on intact amniotic membrane ex vivo. Arch Ophthalmol. 2002 Jun;120(6):783-90.
3. Allen, Claire L et al. "Augmented dried versus cryopreserved amniotic membrane as an ocular surface dressing. PLoS One. 2013;8(10):e78441.
4. Farhadihosseinabadi B, Farahani M, Tayebi T, et al. Amniotic membrane and its epithelial and mesenchymal stem cells as an appropriate source for skin tissue engineering and regenerative medicine. Artif Cells Nanomed Biotechnol. 2018;46(sup2):431-440.
5. Jirsova K, Jones GLA. Amniotic membrane in ophthalmology: properties, preparation, storage and indications for grafting-a review. Cell Tissue Bank. 2017 Jun;18(2):193-204.
6. Dua HS, Gomes JA, King AJ, Maharajan VS. The amniotic membrane in ophthalmology. Surv Ophthalmol. 2004;49(1):51-77.