Comparison of cryopreserved amniotic membrane grafts versus dry amniotic membrane grafts combined with intraoperative mitomycin C for primary pterygium excision using fibringlue technique

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Objective: To compare the recurrence rate of cryopreserved amniotic membrane (cryo AM) grafts and dry amniotic membrane (dry AM) grafts after primary pterygium excision combined with intraoperative mitomycin C (MMC) using fibrin glue technique at 1 year follow up.

Design: Prospective randomized controlled trial

Methods: A prospective randomized controlled trial was conducted in 39 subjects with primary pterygium that were enrolled and randomized into 2 groups, 19 eyes in the cryo AM group, and 20 eyes in the dry AM group. In patients with primary pterygium underwent pterygium excision, 0.02% MMC was applied to the scleral bed. Amniotic membrane was attached using the fibrin glue technique. The measured outcome was recurrence rate at 1 year.

Results: The recurrence rate after pterygium excision with cryo AM and dry AM grafts were 5.26% and 5% respectively. There was no significant difference in the recurrence rate between the 2 groups ($p = 0.839$).

Conclusion: This study provides preliminary evidence that dry AM grafts were effective as cryo AM grafts in adjunctive of pterygium excision to reduce the post operative recurrence.

Conflicts of interest: None

Keywords: Pterygium, Amniotic membrane (AM), Amniotic membrane transplant (AMT), Fibrin glue.

EyeSEA 2018 ; 13(2) : 14-19
Full text. https://www.tci-thaijo.org/index.php/eyesea/index

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Introduction

Pterygium is a common ocular surface disease worldwide especially in South East Asia, an equatorial tropical zone. Surgical techniques have been developed over the past decade ranging from the simple excision to the primary closure, pedicle flap,

transposition of pterygium head or adjunctive treatment with beta radiation or mitomycin C. These modalities can result in decreased recurrence and can be associated with long term complications. Pterygium excision with amniotic membrane graft or combined with intraoperative 0.02% MMC applied 2 - 5 minutes showed lower rate of recurrence were reported.[2,3,9,17,23,25] The dry preserved amniotic membrane has been popular for treatment of cornea surface disease and readily usable with anti-antigenic and epithelialization promoting properties. Advantages of dry AM are sterile, easy for transportation and can be storage at room temperature. Previous usage have reported about good biocompatibility and less recurrence rates (3.0-9.5%) after excision pterygium surgery.[9,10,19,23,26,27] There was no study about use of dry AM for treatment of pterygium in Thailand. This study was intended to evaluate the recurrence of primary pterygium after dry AM transplantation compared with cryo AM using fibrin glue technique.

Materials and Methods

The 39 subjects from Bangkok Metropolitan Administration hospital and 2 private hospitals with primary pterygium were enrolled to this study.

Inclusion Criteria

- Patients who were diagnosed with nasal primary pterygium.
- Age between 30 - 80 years old.

Exclusion Criteria

- Patients who had diagnosed for glaucoma.
- Patients who had more than one headed pterygium.
- Patients can't follow up at 1 year.

All of the patients underwent complete eye examinations under slit lamp biomicroscope. Grading of pterygium was classified by the length of pterygium head measured from limbus to cornea in millimeters.[2,26]

- Grade 1 length of pterygium not more than 3 mm.
- Grade 2 length of pterygium more than 3 mm but less than 5 mm.
- Grade 3 length of pterygium more than 5 mm.

Patients were randomized in 2 groups by mixed block randomization.

There were 19 eyes in cryo AM group and 20 eyes in dry AM group.

Pterygium excisions were surgery on an outpatient service by one surgeon under local anesthesia. After removal of pterygium, 0.02% (0.2mg/ml) MMC was applied over corneo-sclera area for 2 minutes and then irrigate with 20 ml of 0.9% normal saline. The Amnio TEK ™ is an amniotic membrane processed by air drying, UV irradiation for 18-24 hours and stored in sterile single use package. We used cryo AM from Red Cross organization of Thailand in this study to compare recurrence rate between groups. We used amniotic membrane and cut to match size of excised area. The amniotic membrane was attached to sclera bed with fibrin glue (Tissel). Post operative topical medications were tobramycin (Tobrex) four times a day and 1% predisolone acetate (Pred-forte) six times a day for 2 weeks then fluorometholone (FML) four times a day for 1 month. The follow up appointments were on 1 day, 2 weeks, 1 month, 2 months, 6 months and 1 year after surgery. Recurrence was defined as the regrowth of fibrovascular proliferation tissue invading on the cornea. The recurrence was usually occurred in about 12 months.[28,29] The outcome measured in this study is the recurrence rate of pterygium between two groups at 1 year.

Statistic analysis

Demographic data was presented by

descriptive statistics. Categorical data was presented by percentage and continuous data was presented by mean and standard deviation (SD) for all normal distribution. Age was compared by Independent t-test, categorical variables and recurrent rates at 1 year were compared by Chi-square test. Length of pterygium were compared by using Mann-Whitney U test and grading of pterygium was performed by Fisher's exact test. The data were analyzed using software (SPSS, SPSS Inc, Chicago, IL). $p<0.05$ was considered statistically significant.

Results

The characteristics of patients in the 2 groups were compared in Table1. Total of 39 eyes were randomly assigned, 19 eyes in cryo AM group and 20 eyes in dry AM group. There are 7 males (36.84%) and 12 females (63.16%) in cryo AM group. There are 8 males (40%) and 12 females (60%) in dry AM group. The patients' age ranged from 33 to 78 years old, mean age was 53.05 ± 13.77 years in cryo AM group and 53.00 ± 11.83 in dry AM group. There were no statistically significant difference regarding sex (p=0.839), age (p=0.990) among the 2 groups. In grade 1, there are 9 eyes (47.37%) in Cryo AM group and 17 eyes (85%) in Dry AM group. In grade 2, there are 9 eyes (47.37%) in Cryo AM group and 2 eyes (10.0%) in Dry AM group. In grade 3, there is 1 eye (5.26%) in cryo AM group and 1 eye (5.0%) in dry AM group. Severity of pterygium was different in 2 groups (p=0.032), where grade 1 in dry AM group (85.0%) more than cryo AM group (43.37%) and grade 2 in cryo AM group (47.37%) more than dry AM group (2%).

In cryo AM group, recurrence occurred in 1 eye (5.26%) in 2 months. In dry AM group, recurrence occurred in 1 eye (5%) in 2 months. There was no statistically significant difference in the recurrence rate between two groups (p=0. 839).

Discussion

Pterygium is a disease characterized by wing shaped fibrovascular proliferation on the cornea. The pathogenesis is strongly correlated with factors such as UV-light exposure, exposure to dust, wind or other irritants that cause chronic inflammation and ocular surface disease such as dry eye disease. The primary concern in successful pterygium surgery is the recurrence defined by regrowth of the fibrovascular tissue across the limbus onto the cornea. The hypothesis of recurrence is postulated to be a postoperative inflammation period where hyperproliferation of conjunctival fibroblast and over expression of cytokines and metalloproteinase are causative factors.[11,13] Amniotic membrane contains various matrix proteins, which promotes epithelial cell migration and adhesion and has an anti-inflammatory effect. Amniotic membrane promotes re-epithelialization and inhibition of fibrosis.[19,20,23] Amniotic membrane has been successfully used in treatment of cornea surface disease and pterygium surgery.[1,2,19,20,23] This combined low dose intraoperative MMC resulted in decreased recurrence rates following pterygium surgery.[3,4,5,6,7] The advantages of dry AM over cryo AM are sterile tissue, ease of usage and long term storage at room temperature. The dry AM has biocompatibility with the human ocular surface after transplant for excision pterygium.[9,20,23,26] Although dry AM may have lost several characteristics during the dry process[9], combined use of low dose 0.2%MMC intraoperative treatment strongly suppresses postoperative fibrosis in the transplanted area. The recurrence rate in conjunctival autograft was reported 5-7%[8,11,14,15] while amniotic graft was 10-15%[1,8,11,12,13] and amniotic graft combined with dilute intraoperative MMC was 5-8%.[2,3,4,5,6,7] There was no different in recurrence rate in using fibrin glue versus 8-0 vicryl sutures with cryo AM in pterygium surgery, 9.4% in fibrin

glue group and 10.5% in suture group (p=0.33).[18] There were reported for dry AM to treatment of pterygium with successful.[19,23,26,27]

In this study, the recurrence in cryo AM group recurrence occurred in 1 eye (5.26%) and dry AM group recurrence occurred in 1 eye (5%) in 2 months. There was no statistically significant difference in the recurrence rate among two groups (p=0.839). There was also no statistically significant difference in mean age between 2 groups (p=0.990).

The dry AM demonstrated good biocompatibility and effective as cryo AM for pterygium surgery. The low recurrence rate in this study may be from using intraoperative MMC. There was significant difference in severity of pterygium between groups, but there are many factors involved in recurrence rates such as age group, ethnicity, severity of pterygium at presentation, surgeon, surgical technique, anti fibrosis agent (MMC), postoperative medications, patient compliance and environment.

This study was limited in small group of patients, few of recurrence pterygium so we can't analyze factors involved in recurrence of pterygium. Large prospective randomized studies are required to evaluate the long term efficacy on the use of dry AM in reducing the recurrence rate.

Conclusion

This study provides preliminary evidence that dry AM grafts were effective as cryo AM grafts in adjunctive of pterygium excision to reduce the post operative recurrence.

Table 1: Demographic and clinical data of patients

	Cryo AM (n=19)	Dry AM (n=20)	*p*-Value
Sex			0.839
Male	7 (36.84%)	8 (40%)	
Female	12 (63.16%)	12 (60%)	
Age			
Mean±SD(Min, Max)	53.05±13.77(33-78)	53.00±11.83(35-72)	0.990
Side			
Right eye	10 (52.63%)	7 (35.0%)	
Left eye	9 (47.37%)	13 (65.0%)	
Length of pterygium(mm)			
Median(Min,Max)	4 (2.5,6)	3 (2,6)	0.062
Grading of pterygium			0.032
Grade 1	9 (47.37%)	17 (85.0%)	
Grade 2	9 (47.37%)	2 (10.0%)	
Grade 3	1 (5.26%)	1 (5.0%)	
Recurrence rate 12 months	1 (5.26%)	1 (5.0%)	0.839

Table 2: Characteristics of recurrence cases & clinical outcome

Case	Age	Gender	Eye	AM type	Grade	Recurrence time
1	38	F	LE	Cryo AM	2	2 Months
2	40	M	LE	Dry AM	2	2 Months

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