

## Observational Study on Effect of Application of Amniotic Membrane Graft in Patients with Ocular Surface Disorders

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Conflict of interest: Nil

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### Abstract

**Background:** In this study, we wanted to evaluate the effect of amniotic membrane graft in patients with ocular surface disorders.

**Materials and Methods:** This was a hospital based observational study conducted among 50 patients who presented with ocular surface disorders to the OPD of Department of Ophthalmology at Government Rajaji Hospital, Madurai, over a period of one year from 2020 to 2021, after obtaining clearance from Institutional Ethics Committee and written informed consent from the study participants.

**Results:** The tear break-up time (TBUT) value among 50 cases of various ocular surface disorders (P value was < 0.001) was significant. In the improvement of symptoms after amniotic membrane transplantation among 50 cases with ocular surface disorders, the p value was < 0.001 which is significant. When in the presence or absence of epithelialisation after amniotic membrane transplantation among 50 cases of patients with ocular surface disorders, the p value was < 0.001 which is significant. In the evaluation of healing of corneal ulcer, the p value was 0.024 which is significant. In the evaluation of recurrence in pterygium cases, the P value was 0.010 which is significant.

**Conclusion:** It was found that amniotic membrane grafting has benefits like no immunological reaction, cost effective, readily available and had fewer complications. Since vision improvement by amniotic membrane graft (AMG) grafting is a temporary one, ultimately patients needed other mode of surgeries. In institutions where AMG is available, we can use it as a temporary measure till cornea is available for keratoplasty.

**Keywords:** Application, Amniotic, Membrane, Graft, Patients, Ocular Surface, Disorders.

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## Introduction

The vital component of vision is the surface of the eye. Cornea is the major refractive surface of the visual system. The corneal transparency enables light to proceed through the lens and onto the retina for photoreceptor activation. The maintenance and protection of the refractive surface of the cornea is the function of the ocular surface system. The ocular surface includes cornea and conjunctiva, bordered by the upper and the lower lids. A stable tear film plays a key role to maintain the ocular surface health. Patients with ocular surface diseases suffer from discomfort, loss of vision, infection, erosion, ulceration. Among ocular surface disorders, corneal ulcers and pterygium are difficult to treat. If ulcers are not covered promptly, they will result in endophthalmitis and visual loss. Pterygium often recurs after excision. There are other methods of treating these conditions such as occlusion of puncta, tarsorrhaphy, conjunctival flap, anterior stromal puncture and phototherapeutic keratectomy, ocular surface transplantation such as conjunctival autograft and limbal stem cell transplantation. The increased use of amniotic grafts in ophthalmology has changed with better outcomes in managing the ocular surface disease.

### Aims and Objectives

- To observe the effect of amniotic membrane graft in patients with ocular surface disorders.
- To assess the epithelialisation of corneal surface in persistent epithelial defect.
- To assess the healing of corneal ulcer after amniotic membrane grafting.
- To assess the recurrence in cases of pterygium after amniotic membrane grafting.

- To assess the visual outcome in ocular surface disorder patients undergoing amniotic membrane graft.
- To assess the healing in cases of Stevens - Johnson syndrome after amniotic membrane grafting.

### Materials and Methods

This was a hospital based observational study conducted among 50 patients who presented with ocular surface disorders to the OPD of Department of Ophthalmology at Government Rajaji Hospital, Madurai, over a period of one year from 2020 to 2021, after obtaining clearance from Institutional Ethics Committee and written informed consent from the study participants.

### Inclusion Criteria

Patients with neurotrophic keratitis and persistent epithelial defects, impending perforation or perforated corneal ulcers, band keratopathy, bullous keratopathy, after the excision of a conjunctival mass and pterygium, ocular surface reconstruction in symblepharon, acute chemical injury, and chronic limbal deficiency, Steven-Johnson syndrome. - Patient gives consent for study and treatment

### Exclusion Criteria

Patients for whom corneal or scleral graft was available.

Patient does not give consent for the study or refuses the treatment.

### Statistical Methods

Data was entered in MS excel and analysed using Statistical Package for Social Sciences (SPSS) software. Results were presented as tables.

### Results

**Table 1: Demographic Distribution**

Age Distribution		
Age	No of Cases	Percentage
≤ 40	5	10
41 - 50	9	18
51 – 60	23	46
> 60	13	26
Total	50	100
Mean	5	4.14
SD	9	0.75
Sex Distribution		
Gender	No of Cases	Percentage
Male	33	66
Female	17	34
Total	50	100

The age distribution in ocular surface disorders. Among 50 cases, 5 cases belonged to the age group of < 40 years, 9 cases belonged to the age group of 41 – 50 years, 23 cases belonged to the age group of 51 – 60 years, 13 cases belonged to > 60

years with a mean age of 54.14 and SD 9.75.

The sex distribution in this study group, 33 were male and 17 were females. That is 66 % were male and 34% were female.

**Table 2**

<i>Comparison of pre-op and post-op vision</i>						
Evaluation of VA	Pre-Op	Post op				
		1 <sup>st</sup> Week	1 <sup>st</sup> Month	3 <sup>rd</sup> Months	9 <sup>th</sup> Months	1 Year
hm+	5	1	1	1	0	0
1/60	0	1	1	1	0	0
2/60.	2	1	1	1	0	0
3/60.	4	4	4	7	0	0
6/18.	3	0	0	0	0	0
6/24.	9	3	3	3	7	7
6/36.	14	22	22	18	20	22
6/60.	11	18	18	19	11	6
5/60.	0	0	0	0	1	0
6/9.	2	0	0	0	0	0
No follow up	0	0	0	0	11	15
Total	50	50	50	50	50	50
<b>p Value</b>	<b>&lt; 0.001 significant</b>					
<i>Comparison of Fluorescein Stain in Pre-op and Post-op</i>						
s/l/e. Fluorescein Stain	PRE-OP	Post op				
		1 <sup>st</sup> Week	1 <sup>st</sup> Month	3 <sup>rd</sup> Months	9 <sup>th</sup> Months	1 Year
Yes	32	7	8	8	5	4
No	18	43	42	42	34	31
No follow up	0	0	0	0	11	15
Total	50	50	50	50	50	50
<b>p value</b>	<b>&lt; 0.001 significant</b>					
<i>Schirmer's test value</i>						

Schirmer's-test	Pre-op	post op				
		1 <sup>st</sup> week	1 <sup>st</sup> month	3 <sup>rd</sup> months	9 <sup>th</sup> months	1year
t 0	0	0	0	0	0	0
3	6	0	0	0	0	0
4	5	6	6	6	3	1
5	7	6	5	5	5	4
6	14	10	9	9	8	5
7	12	13	13	13	10	7
t 8	6	15	17	17	13	18
No follow up	0	0	0	0	11	15
Total	50	50	50	50	50	50
p Value	< 0.001 significant					

The comparison of pre-op and post-op vision among 50 cases of ocular surface disorders. Pre-operatively, 11 patients had vision of HM + to 3/60, 11 patients had vision of 4/60 to 6/60, 14 patients had vision of 6/36, 9 patients had vision of 6/24, 3 patients had vision of 6/18 and 2 patients had vision of 6/9.

Post-operatively during 1<sup>st</sup> week and 1<sup>st</sup> month, 7 patients had vision of HM + to 3/60, 18 patients with 4/60 to 6/60, 22 patients with 6/36, 3 patients with 6/24. In the 3<sup>rd</sup> month and 9<sup>th</sup> month, HM+ to 3/60 vision was 10 and nil, 4/60 to 6/60 was 19 and 12. 6/36 was 18 and 20, 6/24 was 3 and 7.11 patients had lost the follow up in the 9<sup>th</sup> month. At the end of 1 year of follow up, 6 patients had vision of 4/60 to 6/60, 22 patients with 6/36, 7 patients with 6/24, and 15 patients lost the follow up.

Among 50 cases, fluorescein stain was taken in 32 cases and not taken in 18 cases pre-operatively. In the first week of post-operative period, stain was taken in only 7 cases and not taken in 43 cases. In the first month of post-operative period, stain was taken in 8 cases and not taken in 42 cases.

The Schirmer's value pre-operatively and post-operatively. Schirmer's grading is severe dry eyes – 0 - 5 mm, moderate - 5 - 10 mm, mild – 10 - 15 mm and greater than 15 mm of wetting is normal tear function. Among 50 cases pre-operatively, 18 cases presented with severe dry eye and 32 cases with moderate dry eye. Post-operatively on follow up during 1<sup>st</sup> week, 22 cases with Schirmer's value of 6 - 10 mm and 28 cases with 10 - 15 mm. In the 1<sup>st</sup> month of post-operative period, 20 cases had Schirmer's value of 6 - 10 mm and 30 cases with value of 10 - 15 mm.

**Table 3**

<i>Comparison of the TBUT Pre and Post-operatively</i>						
TBUT-in sec	Pre-op	Post op				
		1 <sup>st</sup> Week	1 <sup>st</sup> Month	3 <sup>rd</sup> Months	9 <sup>th</sup> Months	1 Year
t 0	0	0	0	0	0	0
3	9	1	1	1	0	0
4	6	6	6	3	1	1
5	13	10	9	11	9	4
6	16	15	14	17	14	9
7	6	14	16	16	14	17
t 8	0	4	4	2	1	4
No follow up	0	0	0	0	11	15
Total	50	50	50	50	50	50

<b>p value</b>	<b>&lt; 0.001 significant</b>				
<b><i>The improvement of symptoms</i></b>					
<b>Evaluation</b>	<b>post op</b>				
<b>Improvement in Symptoms</b>	<b>1<sup>st</sup>week</b>	<b>1<sup>st</sup>month</b>	<b>3<sup>rd</sup>months</b>	<b>9<sup>th</sup>months</b>	<b>1year</b>
Yes	48	48	44	36	31
No	2	2	6	3	4
No follow up	0	0	0	11	15
Total	50	50	50	50	50
<b>p value</b>	<b>&lt; 0.001 significant</b>				
<b><i>The Presence or Absence of Epithelialisation</i></b>					
<b>Evaluation</b>	<b>post op</b>				
<b>Epithelialisation</b>	<b>1<sup>st</sup> Week</b>	<b>1<sup>st</sup> Month</b>	<b>3<sup>rd</sup> Months</b>	<b>9<sup>th</sup> Months</b>	<b>1 Year</b>
Yes	40	41	40	39	35
No	10	9	10	0	0
No follow up	0	0	0	11	15
Total	50	50	50	50	50
<b>p value</b>	<b>&lt; 0.001 significant</b>				

The TBUT value among 50 cases of various ocular surface disorders, the TBUT is categorised into normal - > 10 seconds, marginally dry eye - 5 - 10 seconds, poor - < 5 seconds. Among 50 cases, 15 cases had TBUT value of < 5 seconds and 35 cases had value of 5 - 10 seconds in the 1<sup>st</sup> week of post-operative period. In the 1<sup>st</sup> month of post-operative period, 49 patients had marginal TBUT value of 5 - 10 seconds and only one patient had < 5 seconds. P value is < 0.001 which is significant.

The improvement of symptoms after amniotic membrane transplantation among 50 cases with ocular surface disorders. In the 1<sup>st</sup> week of post-operative period, 48 cases had improvement in symptoms and 2 cases had no improvement in symptoms. In the 1<sup>st</sup> month of post-operative period, 48 cases had improvement in symptoms and only 2 cases had no improvement in

symptoms. In the 3<sup>rd</sup> month, 44 cases had improvement and 6 had no improvement. In the 9<sup>th</sup> month, 36 cases had improvement, 3 cases had no improvement and 11 cases had lost the follow up, p value is < 0.001 which is significant.

The presence or absence of epithelialisation after amniotic membrane transplantation among 50 cases of patients with ocular surface disorders. In the first week of post-operative period, 40 cases had epithelialisation and 10 cases had no epithelialisation. In the 1<sup>st</sup> month, 41 cases had epithelialisation and 9 cases had no epithelialisation. In the 3<sup>rd</sup> month, 40 cases had epithelialisation and 10 cases were with no epithelialisation. In the 9<sup>th</sup> month, 39 cases had epithelialisation and 11 cases had lost the follow up. In 1 year follow up, 35 cases had epithelialisation and 15 cases had lost the follow up, p value is < 0.001 which is significant.

Table 4

<i>The Evaluation of Healing of Corneal Ulcer</i>					
<b>Evaluation</b>	<b>Post op</b>				
<b>Healing of Corneal Ulcer</b>	<b>1<sup>st</sup> Week</b>	<b>1<sup>st</sup> Month</b>	<b>3<sup>rd</sup> Months</b>	<b>9<sup>th</sup> Months</b>	<b>1 Year</b>
Yes	13	13	13	8	8
No	8	8	8	8	8
No follow up	0	0	0	5	5
Total	21	21	21	21	21
<b>p value</b>	<b>0.024 significant</b>				
<i>The Evaluation of Recurrence in Pterygium Cases</i>					
<b>Evaluation</b>	<b>Post op</b>				
<b>Recurrence in Pterygium Cases</b>	<b>1<sup>st</sup> Week</b>	<b>1<sup>st</sup> Month</b>	<b>3<sup>rd</sup> Months</b>	<b>9<sup>th</sup> Months</b>	<b>1 Year</b>
Yes	3	3	3	3	3
No	8	8	8	3	3
No follow up	0	0	0	5	5
Total	11	11	11	11	11
<b>p value</b>	<b>0.010 Significant</b>				

The evaluation of healing of corneal ulcer. Among 21 cases with corneal ulcer, in the 1<sup>st</sup> week of post-operative period, 13 cases had healing of corneal ulcer and in the 1<sup>st</sup> month, 13 cases had healing of corneal ulcer. In the 3<sup>rd</sup> month, 13 cases had healing of corneal ulcer and in the 9<sup>th</sup> month, 8 cases and in the 1 year, 8 cases had healing of corneal ulcer. P value is 0.024 which is significant.

The evaluation of recurrence in pterygium cases. Among 11 pterygium cases, 3 patients had recurrence and 8 patients had no recurrence in the first week, 1<sup>st</sup> month and 3<sup>rd</sup> month. In the 9<sup>th</sup> month and 1 year follow-up, 3 patients had recurrence, 3 with no recurrence and 5 patients had lost to follow up. P value is 0.010 which is significant.

### Discussion

In our study, we had observed the effect of amniotic membrane graft in patients with ocular surface disorders. We assessed the epithelialisation of corneal surface in persistent epithelial defect, healing of corneal ulcer after AMG, recurrence in cases of pterygium after AMG, visual outcome in ocular surface disorder patients undergoing amniotic membrane graft, healing in cases of Stevens-Johnson

syndrome after amniotic membrane grafting.

In our study, the demographic characteristics among 50 cases shows that 5 cases belong to < 40 years, 9 cases belong to 41 – 50 years, 23 cases belong to the age group of 51 – 60 years, 13 cases belong to > 60 years with a mean age of 54.14 and SD 9.75.

In our study, 33 males and 17 females with ocular surface disorders were included which is similar to study conducted by N.N. Ashraf, M.I. Adhi et al. [1]

Among 50 cases with ocular surface disorders, 11 patients with pterygium, 1 with Steven Johnson syndrome, 1 case with corneal perforation, 3 cases with chemical injury, 4 cases with descemetocoele, 2 cases with corneal thinning, 5 cases with persistent epithelial defect, 3 with neurotrophic keratitis, 5 with non-healing corneal ulcer, 1 with non-healing fungal corneal ulcer, 2 with impending perforation, 1 with fungal corneal ulcer, 1 with marginal keratitis, 2 cases with pseudophakic bullous keratopathy, 5 with spheroidal generation and 3 cases with symblepharon were included which is similar to study conducted by Shreya et al. [2]

In this study, duration of complaints was divided into two groups of complaints with < 7 days and > 7 days. 35 patients were presented with < 7 days and 15 with > 7 days of complaints.

In this study, the vision outcome after amniotic membrane graft transplantation was compared with pre-operative vision. There was significant vision improvement after AMG grafting. The p value is < 0.001 significant which is similar to study conducted by J.H. Park et al. [3]

While treating ocular surface disorders, it is important to do dry eye evaluation. A thorough assessment of the ocular surface system anatomy and function can be performed using history of illness, patient symptoms, traditional clinical tests, the newly described TFOD, or by using instruments to obtain quantitative measurements. In this study, patients were evaluated by doing Schirmer's test, TBUT and fluorescein staining pre-operatively and post-operatively which is similar to study conducted by Gheorghe A et al. [4]

Among 50 cases, stain was taken in 32 cases and not taken in 18 cases preoperatively. In the post-operative period, 4 cases had taken stain, 31 were not taken and 15 were lost follow up at the end of 1 year. p value is <0.001 which is significant.

Schirmer's test showed 18 cases with severe dry eye and 32 cases with moderate dry eye pre-operatively. Post operatively at the end of 1 year, 5 patients had severe dry eye, 30 patients had moderate dry eye and 15 patients had lost the follow up p value is < 0.001 which is significant.

In this study, TBUT comparison on pre-op and post-op evaluation was done. 15 patients with severe dry eye and 35 patients with marginal dry eye were presented before AMG grafting. At the end of 1 year of follow up after AMG grafting, it was found that 5 cases had severe dry eye, 30 with moderate dry eye

and 15 had lost the follow up p value is < 0.001 which is significant.

Patients had AMG grafting as per the above protocol. Improvement of symptoms was compared before and after AMG grafting. It was found that there was immediate improvement in pain, redness, vision and irritation. In the 1st week, 48 patients had improvement in symptoms and 2 patients had no improvement. At the end of 1 year, 31 patients had improvement, 4 with no improvement and 15 had lost the follow up. p value is < 0.001 which is significant which is similar to study conducted by N.N. Ashraf, M.I. Adhi et al. [1]

In this study, it was found that AMG has promoted re-epithelialisation among corneal ulcer patients. The p value is < 0.001 which is significant and similar to the study conducted by N.N. Ashraf, M.I. Adhi et al. [1]

In this study among 21 cases with corneal ulcer, it was found that 13 cases had immediate response of healing. At the end of 1 year of follow up, 8 cases had healing and 8 had no healing of corneal ulcer and 5 had lost the follow up. P value is 0.024 which is significant Chen et al. [5]

Out of 11 patients with pterygium, 3 of them had recurrence immediately and 8 patients had no recurrence. In the follow up of 1 year, 3 had recurrence, 3 with no recurrence and 5 with no follow up Rosen et al. [6]

### Conclusion

Amniotic membrane grafting is an easier and safest procedure in ocular surface disorders. This study includes various ocular surface disorders with poor vision, pain, redness, irritation and epithelial defect. It was observed that there was tremendous improvement in symptoms like redness, photophobia and pain after AMG grafting. Initially, there was good visual outcome after AMG grafting in the ocular surface disorders. Later on depending upon

the aetiology of the disease, vision deterioration has occurred. Those patients were in need of other mode of surgeries. AMG has promoted epithelialisation in the persistent epithelial defect, corneal ulcer cases. Patients with corneal ulcer showed improvement in symptoms with reduced inflammation, healing of ulcer with epithelialisation and improvement in vision. Among 21 cases with corneal ulcer, 8 cases had healing of corneal ulcer and 8 cases with no healing. Patients with no response to AMG grafting needed other modalities of treatment like keratoplasty. Epithelialisation was observed among 40 cases with ocular surface disorders initially. Remaining 10 cases needed repeat procedure or other mode of surgeries. Patients with Steven Johnson syndrome and chemical injury shows improvement in symptoms initially but later on developed vascularisation and condition has worsened. Those patients required keratoplasty. Recurrence of pterygium was assessed in this study and was found that recurrence was less with AMG grafting. Among 11 cases, 3 patients had recurrence and they needed repeat surgery. From this study, it was found that amniotic membrane grafting has benefits like no immunological reaction, cost effective, readily available and had fewer complications. Since vision improvement by AMG grafting is a temporary one, ultimately patients needed other mode of

surgeries. In institutions where AMG is available, we can use it as a temporary measure till cornea is available for keratoplasty.

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