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COMPARISON OF PRIMARY GRAFT FAILURE AFTER PENETRATING KERATOPLASTY WITH OPTISOL PRESERVED CORNEA GRAFTED WITHIN 07 DAYS VERSUS GRAFTED BETWEEN 07-14 DAYS

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ABSTRACT

Background: Every ophthalmic surgeon who performs penetrating Keratoplasty has experienced the disappointment felt by patient and physician alike when a technically successful corneal graft fails. Despite the advances that have been made in corneal preservation and surgical technique, a significant proportion of grafts eventually fail.
Objective: To compare frequency of graft failure after penetrating Keratoplasty with Optisol preserved cornea in two groups i.e. cornea preservation time less than 7 days versus cornea preservation time from 7 to 14 days
Study Design: Randomized control trial
Study Setting: Department of Ophthalmology, FMU Allied Hospital Faisalabad
Study Duration: 6 months after approval of the synopsis From: June 2024 to November 2024
Methodology: Informed consent was taken from all patients. Patient fulfilling the inclusion criteria were enrolled from OPD of Ophthalmology unit. Detailed

history and physical examination was done. Patients were divided in two groups by lottery method. Patients in Group A were grafted with corneas preserved in Optisol medium within 7 days and Patients Group B were grafted with corneas preserved in Optisol medium from 7 to 14 days after harvesting from the donor. All corneal grafts were done by single surgical team under standard surgical procedure. Post-operative care was done for all patients according to standard protocols of hospital. Patients were examined for graft failure at follow-up visit at 12 weeks after cornea graft procedure.

Results: In this study, mean age was 50.8±8.59 years in Group-A and 48.35±9.57 years in Group-B, 65%(n=26) Patients in Group-A and 60%(n=24) Patients in Group-B were male and 35%(n=14) in Group-A and 40%(n=16) in Group-B were females. Comparison of graft failure shows 7.5%(n=3) in Group-A and 47.5%(n=19) in Group-B had graft failure whereas 92.5%(n=37) in Group-A and 52.5%(n=21) in Group-B had no graft failure, (p value of 0.00006.)

Conclusion: Cornea preservation in Optisol medium within 7 days had significantly lower rate of graft failure when compared with cornea preservation time of 7 to 14 days in cases undergoing penetrating Keratoplasty.

INTRODUCTION

Penetrating Keratoplasty (PKP) is a full-thickness Corneal transplant procedure, in which a trephine of an appropriate diameter is used to make a full-thickness resection of the patient's cornea, followed by placement of a full-thickness donor corneal graft. The major indications for penetrating corneal transplantation being keratoconus, bullous keratopathy, corneal opacity, corneal dystrophy and history of previous failed ipsilateral corneal graft. PKP has proven to be one of the most successful and frequently performed transplantation procedures in recent years. According to some recent studies, the 10-year corneal graft survival rate is 36% and in some it is up to 89%.(1,2) Despite the relatively high survival rates of corneal transplants the cumulative number of graft failures still remains significant. The proposed risk factors for Primary graft failure include donor age > 70 years, trauma as a cause of death, a death to preservation time of over 12 hours, and a storage time of greater than 7 days.(3) Graft failure can be attributed to the number of endothelial cells provided by the graft which is evident in many studies suggesting that late graft failure can be avoided if the graft provided the highest number of viable endothelial cells.(4). The prolonged storage of donor cornea reduces the endothelial cell density, which is also affected by storage technique and donor age. It has been shown that little endothelial cell loss occurs during donor cornea storage in a solution containing chondroitin sulphate (Optisol) for up to 14 days, which also allows successful sharing of imported corneas.(5) Thus to reduce the risk of primary graft failure, the recommended storage periods are kept far below the suggested maximum limits i.e. 2-3 days for M-K medium and 7-10 days for Optisol.(6,7) Patients within 7 days or less of initial symptoms had better visual recovery, corneal edema regression and less graft failure ($p<0.001$).(8) In one international study it was estimated that cornea graft failure rate was increased with increased preservation time i.e. 5% (if the donor cornea was preserved for 7 days) to 53% (if preserved for 8 to 14 days).(5) It is noticed that cornea preservation time affects the outcome of cornea graft. Prolonged preservation time can increase the risk for graft failure but till date we have no data for our local population. The rationale of this study is to find safe cornea preservation time for our local population so that risk

of graft failure can be reduced. After concluding results of our study we will be able to determine cornea preservation time so that graft procedure can be made more safe for our patients.

MATERIALS AND METHODS

This randomized control trial was conducted in the Department of Ophthalmology at Allied Hospital, Faisalabad Medical University (FMU), Faisalabad, from July 2019 to January 2020. The sample size was calculated using the WHO sample size calculator for two proportions, with an assumed proportion of graft failure (P1 = 5% and P2 = 53%), a study power of 90%, and a significance level of 5%. The estimated sample size was 80 patients, with 40 participants in each group. Non-probability consecutive sampling was used for patient selection. Patients aged 30 to 70 years of both genders undergoing penetrating keratoplasty, as diagnosed through history and slit lamp examination, were included in the study. Exclusion criteria comprised eyes undergoing regrafting (confirmed via medical records and patient history), subjects with preoperative central subepithelial or stromal scarring (assessed via slit lamp examination), and uncontrolled glaucoma (defined as intraocular pressure >25 mmHg, determined through history and tonometry). After obtaining approval from the ethical review board, informed consent was taken from all participants. Eligible patients were enrolled from the Ophthalmology OPD, and a detailed history and physical examination were conducted. Participants were randomly allocated into two groups using the lottery method. Group A received corneas preserved in Optisol within 7 days, while Group B received corneas preserved in Optisol for 7 to 14 days. All surgeries were performed by a single surgical team following standard procedures. Post-operative care adhered to hospital protocols, and graft failure was assessed at a 12-week follow-up visit. Data were recorded in a specially designed proforma, ensuring patient privacy. Data were analyzed using SPSS version 21. Qualitative variables such as gender, eye involvement, and graft failure were expressed as frequencies and percentages, while quantitative variables like age and disease duration were presented as mean ± standard deviation. The chi-square test was used to compare graft failure rates between the two groups. Additionally, data were stratified by age, gender, and disease duration, with post-stratification analysis performed using the chi-square test. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 80 cases (40 in each group) fulfilling the selection criteria were enrolled to compare frequency of graft failure after penetrating Keratoplasty with Optisol preserved cornea in two groups i.e. cornea preservation time less than 7 days versus cornea preservation time of 7 to 14 days. Age distribution shows that 42.5%(n=17) in Group-A and 50%(n=20) in Group-B were between 30-50 years of age whereas 57.5%(n=23) in Group-A and 50%(n=20) in Group-B were between 51-70 years of age, Mean age was 50.8+8.59 years in Group-A and 48.35+9.57 years in Group-B. (Table No. 1)

Table No. 1 Age Distribution
(n=80)

Age (in years)	Group-A (n=40)		Group-B (n=40)	
	No. of patients	%	No. of patients	%
30-50	17	42.5	20	50
51-70	23	57.5	20	50
Total	**40**	**100**	**40**	**100**
Mean±SD	**50.8±8.59**		**48.35±9.57**	

Gender distribution shows that 65%(n=26) in Group-A and 60%(n=24) in Group-B were male and 35%(n=14) in Group-A and 40%(n=16) in Group-B were females. (Table No. 2)

Table No. 2 Gender Distribution
(n=80)

Gender	Group-A (n=40)		Group-B (n=40)	
	No. of patients	%	No. of patients	%
Male	26	65	24	60
Female	14	35	16	40
Total	**40**	**100**	**40**	**100**

Mean duration of disease was calculated a 3.48+1.36 months in Group-A and 3.68+1.10 months in Group-B. (Table No. 3)

Table No. 3 Mean Duration Of Disease
(n=80)

Duration (weeks)	Group-A (n=40)		Group-B (n=40)	
	Mean	SD	Mean	SD
	3.48	1.36	3.68	1.10

Frequency of eye involved shows that 50%(n=20) in Group-A and 45%(n=18) in Group-B had right eye whereas 50%(n=20) in Group-A and 55%(n=22) in Group-B had left eye. (Table No. 4)

Table No. 4 Frequency Of Eye Involved
(n=80)

Eye involved	Group-A (n=40)		Group-B (n=40)	
	No. of patients	%	No. of patients	%
Right	20	50	18	45
Left	20	50	22	55
Total	**40**	**100**	**40**	**100**

Comparison of graft failure shows 7.5%(n=3) in Group-A and 47.5%(n=19) in Group-B had graft failure whereas 92.5%(n=37) in Group-A and 52.5%(n=21) in Group-B had no graft failure, p value of 0.00006. (Table No. 5)

Table No. 5 Comparison Of Graft Failure
(n=80)

Graft failure	Group-A (n=40)		Group-B (n=40)	
	No. of patients	%	No. of patients	%
Yes	3	7.5	19	47.5

No	37	92.5	21	52.5
Total	**40**	**100**	**40**	**100**

P value=0.00006

The data was stratified for age, gender and duration of disease. Post stratification chi square test was applied and p <0.05 was considered significant. (Table No. 6)

Table No. 6 Stratification for Graft Failure by Age, Gender, and Duration of Disease (n = 80)

Stratification Variable	Category	Group	Graft Failure: Yes	Graft Failure: No	P Value
Age (years)	30–50	A	1	16	0.001
		B	11	9	
	51–70	A	2	21	0.01
		B	8	12	
Gender	Male	A	2	24	0.002
		B	11	13	
	Female	A	1	13	0.01
		B	8	8	
Duration of Disease	1–3 months	A	1	19	0.0006
		B	10	8	
	>3 months	A	2	18	0.02
		B	9	13	

DISCUSSIONS

Penetrating Keratoplasty (PKP) is a 110-year-old procedure whose effectiveness and safety has led to be the most frequently performed type of transplant worldwide. However, the prolonged storage of donor cornea reduces the endothelial cell density, which is also affected by storage technique and donor age. It has been shown that little endothelial cell loss occurs during donor cornea storage in a solution containing chondroitin sulphate (Optisol) for up to 14 days, which also allows successful sharing of imported corneas.(5) Thus to reduce the risk of primary graft failure, the recommended storage periods are kept far below the suggested maximum limits i.e. 2-3 days for M-K medium and 7-10 days for Optisol.(6,7) This study was designed is to find safe cornea preservation time for our local population so that risk of graft failure can be reduced. And we may be able to determine safe cornea preservation time our patients. In our study, 42.5%(n=17) in Group-A and 50%(n=20) in Group-B were between 30-50 years of age whereas 57.5%(n=23) in Group-A and 50%(n=20) in Group-B were between 51-70 years of age, mean age was 50.8+8.59 years in Group-A and 48.35+9.57 years in Group-B, 65%(n=26) in Group-A and 60%(n=24) in Group-B were male and 35%(n=14) in Group-A and 40%(n=16) in Group-B were females. Comparison of graft failure shows 7.5%(n=3) in Group-A and 47.5%(n=19) in Group-B had graft failure, (p value of 0.00006.) These findings are supported by an international study where the cornea graft failure rate was increased with increased preservation time i.e. 5% (if the donor cornea was preserved within 7 days) to 53% (if preserved for 8 to 14 days).(5) The studies have reported a loss of Class II (HLA-DR) positive epithelial Langerhans cells after corneal preservation in organ culture for l-3 weeks.(9) A preliminary study in rats found that the levels of Class I antigens were diminished in the epithelium and stroma after storage for 5-7 days

at 4°C in intermediate term storage media such as CSM and K-Sol, compared with levels in fresh tissue, tissue preserved for three days at 4" C in MK short-term storage medium, or tissue preserved for 17 days at 37" C in organ culture medium.“' Since Class II antigen-bearing Langerhans cells are thought to play a role in the processing of antigen and the sensitization of the host to non-self-antigens, IgE and Class I antigens elicit strong cellular and humoral responses during allograft rejection, these studies suggest that the method of corneal preservation might influence allograft rejection after penetrating Keratoplasty. A species-specific prolongation of xenograft survival after organ culture has been reported in rabbits, but there are no data to suggest that this applies to allografts. While these studies are suggestive, there is no evidence that the incidence of corneal allograft rejection in humans is influenced by the use of fresh tissue, tissue preserved using any of the currently available cornea; storage media, or tissue preserved in organ culture. The results of our study justify the hypothesis that "there is a difference in primary graft failure after penetrating Keratoplasty with Optisol preserved cornea grafted within 7 days versus grafted after 7 days" however, the studies on this topic are very limited which needs some other studies to validate our results.

CONCLUSION

Optisol Cornea preservation within 7 days had significantly lower rate of graft failure when compared with cornea preservation time of 7 to 14 days in cases undergoing penetrating Keratoplasty with Optisol.

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