ORIGINAL RESEARCH PAPER

Ophthalmology

STUDY OF COMPARATIVE EFFICACY OF TOPICAL CORTICOSTEROID WITH TOPICAL TACROLIMUS OINTMENT & INITIAL TOPICAL CORTICOSTEROID THERAPY IN PENETRATING KERATOPLASTY

KEY WORDS: Withania somnifera , Solanum nigrum , Allelopathy, Pennisteum glaucum(pearl millet)

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ABSTRACT

INTRODUCTION: Topical steroids have been the main stay of treatment for the graft rejection in penetrating keratoplasty since decades but with this effect there comes a plenty of adverse effects too. This made us to compare the efficacy of other immunosuppressive which have lower side effects, with steroids.

PURPOSE: To study the comparative effect of topical Tacrolimus and topical corticosteroid on graft rejection, corneal transparency, corneal vascularization, healing of graft-host junction & intraocular pressure.

DESIGN: Cross-sectional study.

PARTICIPANTS: 60 cases which underwent penetrating keratoplasty for various reasons were studied.

MATERIALS & METHODS: Patients were divided into 2 groups one on Topical Prednisolone 1% & other on combination of 0.03% topical tacrolimus ointment & topical Prednisolone 1% . After discharge, patients were seen weekly for 3 months and then once in a month for next 6 months.

RESULTS: Significant reduction ($p>0.05$) in complications like secondary glaucoma & persistent epithelial defect was observed in our study.

CONCLUSION: We conclude that topical tacrolimus 0.03 % was equally effective to topical prednisolone 1% in reducing the risk of graft rejection & had very low predisposition to complications. Thus topical tacrolimus 0.03% can be considered as an effective modality of treatment in cases of penetrating keratoplasty.

INTRODUCTION:

According to World Health Organization's (WHO; Geneva, Switzerland) definition of blindness, it is estimated that there are currently 45 million people worldwide who are bilaterally blind, of which 6 to 8 million are blind due to corneal diseases. In India there are approximately 6.8 million people who have corneal blindness with vision less than 6/60 in at least one eye, and of these, about 1 million have bilateral corneal blindness. If the present trend continues, it is expected that the number of corneal blind individuals in India will increase to 10.6 million by 2020.[1]Quality of donor material depends on age of donor, cause of death, death-enucleation interval, enucleation - transplantation interval, method and duration of preservation and endothelial cell density. Corneal endothelial cells are essential in maintaining stromal deturgescence, but they are also the prime target of an immune - mediated attack during corneal allograft rejection. The functional status of the corneal endothelial cells is one of the major criteria determining the long term outcomes of corneal transplantation.The importance of corneal grafting lies in the fact that successful transplantation can restore excellent sight to persons suffering from corneal blindness. Penetrating keratoplasty is probably the most frequently performed and most successful form of transplantation.[2]The proportion of corneal blind that could derive long term benefit from corneal grafting depends on graft transparency. Transparency is affected by various factors which include type of donor material, condition of recipient eye, operative procedure and post-operative treatment. Corticosteroids are the mainstay of treatment of corneal graft rejection. But there are many complications & contraindications of steroids[1], which forced the researchers to search new immunosuppressant. Tacrolimus was discovered in 1984; it was among the first macrolide immunosuppressant discovered. It is a 23-membered macrolide lactone discovered from the fermentation broth of a Japanese soil sample that contained the bacteria Streptomyces tsukubaensis[2]. In 1989, Kobayashi et al. first reported that tacrolimus suppressed corneal graft rejection in rabbits. Since then, the use of tacrolimus has been of special interest in ophthalmology because it was shown to be effective in the treatment of immune-mediated diseases such as corneal graft rejection, ocular inflammation, ocular pemphigoid and uveitis[2]. Tacrolimus was first approved by the Food and Drug Administration (FDA) in 1994 for use in liver transplantation; this has been extended to include kidney, heart, small bowel, pancreas, lung, trachea, skin, cornea, bone marrow, and limb transplants[3]. There were many studies & research done on tacrolimus which inspired us & formed the basis of this study.

MATERIALS & METHODS: All patients who had undergone penetrating keratoplasty between March 2015 & October 2016. The study protocol was approved by the institutional review committee. A written informed consent was taken from all the study subjects. All patients & donated eyes underwent standard ocular examination protocol for keratoplasty. Patients were divided into 2 groups one on Topical Prednisolone 1% & other on combination of 0.03% topical tacrolimus ointment & topical Prednisolone 1% . After discharge, patients were seen weekly for 3 months and then once in a month for next 6 months.

OPERATIVE PROCEDURES: The operation was done under local anesthesia. If patient was uncooperative or apprehensive, then the operation was performed under general anesthesia. Donor cornea was prepared by placing entire corneo-scleral button on a Teflon block (after instillation of viscoelastic on the block) with endothelial side up and was punched by trephine of required diameter. Recipient's eye the corneal disc was removed from recipient's cornea using trephine of required diameter (0.5 mm less than that used for graft cornea).In some cases, synechiotomy and removal of exudative membrane was done after the excision of recipient corneal button. Few cases required trimming of edges of recipient cornea. In aphakic cases, where vitreous was present in anterior chamber, vitrectomy or vitreous aspiration was done depending on the consistency of vitreous. A few cases also involved removal of cataract at the time of surgery. The recipient bed was coated with methyl cellulose and the donor button was transferred to the recipient's bed taking care not to traumatize the corneal endothelium or epithelium. Four stay sutures with 8 -0 silk

were applied at 3, 6, 9 and 12 o clock position. Secondary suturing was then done with 10-0 nylon monofilament suture (either interrupted sutures or continuous sutures) Anterior chamber was reformed by ringer lactate solution or air, and wound was tested for any leakage. Antibiotic eye drops were instilled and pad and bandage was done. Postoperatively patients were randomly divided into 2 groups, Group A one on Topical Prednisolone 1% (hourly for 1 week, 6 times a day for 1 month & q.i.d for 6 months) & Group B on combination of 0.03% topical tacrolimus ointment (b.d for 1 month & h.s for 6 months) & topical Prednisolone 1% (6 times a day for 1 week, q.i.d for 1 month & b.d till 6 months). After discharge, patients were seen weekly for 3 months and then once in a month for next 6 months. During each follow up through examination was performed. Patients were started on pulse steroid therapy (i/v methyl prednisolone 1 mg o.d for 3-5 days) in case of signs of rejection.

RESULTS: The paired t test was used to determine any significant difference of prevalence of complications between the two groups. p<0.05 was considered significant. Significant reduction was observed in complications like persistent epithelial defect, secondary glaucoma & cataract (p value >0.05). Difference in final visual outcome in both the groups was not significance.

POST OPERATIVE COMPLICATION	GROUP A		GROUP B	
	No	%	No	%
Suture abscess	28	45%	20	34%
Persistent Epithelial defect	24	40%	17	28%
Vascularisation of cornea	22	37%	20	34%
Corneal infiltration	18	30%	15	25%
Graft rejection	12	20%	10	17%
Secondary glaucoma	10	17%	5	8%
Anterior synechie	6	10%	6	10%
Wound dehiscence	6	10%	4	7%
Graft ectasia	4	7%	3	5%
Corneal abscess	2	3%	0	0%
Cataract	12	20%	5	8%
No complication	8	13%	17	28%

Visual Acuity	Group A		Group B	
	Preop	Postop	Preop	Postop
PL+ HM +	22	8	21	7
CF	5	9	4	9
CF- 3 feet	2	7	5	10
6/60	1	3	-	2
6/36	-	2	-	1
>6/24	-	1	-	1

DISCUSSION: As keratoplasty comprises of intimate relationship between tissue of two individuals, multiple factors are known to regulate or influence the outcome of this surgery. "Although the cornea is classically described as possessing immunological privilege, the protection this affords is only relative and rejection is still the commonest cause of failure." Consequently, immunosuppressant is still routinely used in keratoplasty. Although topical corticosteroids remains the mainstay of treatment of corneal graft rejection, the side effects often preclude the patients from receiving long term topical corticosteroid that are necessary for graft rejection[1,4,5,10]. Therefore, more specific and less toxic agents are needed in the management of keratoplasty[3,9,16,17]. We in our study found significant reduction in post operative complications like secondary glaucoma from 17% to 8% results were comparable to that of Tulio B. Abud, MD et al18. Persistent epithelial defect reduced from 40% to 28% in Group B & our results were comparable to that of Reitamo S et al 8 , Sloper CM et al9, Thomas Reinhard et al10, J.S Dhiliwal et al12. Reduction in other complications like neovascularaization, suture abscess, secondary cataract & comparison of final graft clarity were not significant as found in other studies.

CONCLUSION: We conclude that topical tacrolimus 0.03% was equally effective to topical prednisolone 1% in reducing the risk of graft rejection & had very low predisposition to complications like secondary glaucoma (P value <.05), cataract (P value <.05) or epithelial defect. Thus topical tacrolimus 0.03% can be considered as an effective modality of treatment in cases of penetrating keratoplasty.

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