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Study To Evaluate The Factors Causing Graft Opacification In Penetrating Keratoplasty

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Abstract
Aim: *A cohort study to evaluate the factors that contribute to opacification of a corneal graft following Penetrating Keratoplasty.*
Material and Methods: *This cohort study consisted of 40 patients (40 eyes), of opacified graft after penetrating keratoplasty. Thirty patients were studied retrospective for 5 years and 10 patients prospectively for 2 years. The various clinical parameters in all the cases of opacified grafts were studied and evaluated. Graft opacification was defined as irreversible loss of central graft clarity, irrespective of the level of visual acuity. The time of graft opacification was defined as the visit at which irreversible loss of graft clarity was first documented. Apart from normal ocular and systemic history, history of previous ocular surgery, ocular surface disease, glaucoma or previous penetrating keratoplasty was noted. Ocular examination included recording BCVA, detailed slit lamp examination, fundus evaluation if possible, recording IOP and USG B scan. Follow-up was done daily for a week, then weekly for a month and subsequently monthly for a year. Steroids were continued for an average of 06 months-01 year unless the development of glaucoma prompted us to discontinue steroids. Topical 0.05% Cyclosporine was introduced in all cases to reduce the dosage of topical steroids. Data was collected and statistically analysed.*
Results: *Pre-existing glaucoma is a risk factor for glaucoma in early postoperative period Odds Ratio-2.58). Mc-Carey Kaufman (MK) media had a positive association for graft clarity as compared to moist chamber (Odds Ratio- 2.8).*
Conclusion: *Pre-existing glaucoma is a significant risk factor for post keratoplasty glaucoma resulting in graft opacification, modification of which can improve graft survival and clarity.*
Keywords: *Graft Opacification, Penetrating Keratoplasty, Penetrating Keratoplasty and Glaucoma (PKPG).*

I. Introduction

Corneal Graft Opacification is the greatest limiting factor in the success of corneal graft and Edward Maumenee was the one to recognize this clinical entity. The classic scientific description was explained by Khodadoust. Graft opacification when defined as irreversible loss of clarity, complicates 3% to 20% of penetrating keratoplasties [1,2]. The true success of corneal graft surgery cannot be judged by a single index, but is dependent on a variety of preoperative, intra-operative, and postoperative factors. Comparing survival rates between studies is difficult due to differences in population size and characteristics, follow-up time and definitions of graft failure. In the literature, graft survival ranges between 90% and 97% at 4 years [3,4], 46.5% to 93% at five year depending on the diagnosis [5-7]. Many studies have been done in the past for corneal graft failure and rejection but there are only limited studies for the factors resulting in corneal graft opacification. The purpose of this study was to study cases of corneal graft failure to evaluate the preoperative factors that influence the clarity of the graft and to analyze the postoperative events and complications that result in graft opacification (defined as irreversible loss of graft clarity resulting in visual acuity less than 6/60).

II. Materials and Methods

This ambidirectional study consisted of 40 eyes (40 patients) of opacified corneal grafts after penetrating keratoplasty. 30 patients were studied retrospectively (past 05 years) and 10 patients were studied prospectively for 02 years. The study was done at a tertiary care centre on patients registered with the eye bank that had undergone penetrating keratoplasty in the last 05 years and developed corneal opacity, and those patients who underwent penetrating keratoplasty over the next 02 years and suffered an irreversible opacification of graft. The various clinical parameters in all the cases of opacified grafts were studied and evaluated. Graft opacification was strictly defined as irreversible loss of central graft clarity, irrespective of the level of visual acuity. The time of graft opacification was defined as the visit at which irreversible loss of graft clarity was first documented. All patients with visual acuity of < 6/60 or of 6/60 with evidence of irritable eye with pain and lacrimation severe enough to interfere with daily life were included in the study. Patients with

inaccurate projection of rays, vitreous hemorrhage, optic nerve disease, retinal disorder or retinal detachment were excluded from the study. Apart from normal ocular and systemic history, history of previous ocular surgery, ocular surface disease, glaucoma or previous penetrating keratoplasty was noted. Ocular examination included recording BCVA, detailed slit lamp examination, fundus evaluation if possible, recording IOP and USG B scan (where fundus details were not seen by indirect ophthalmoscope). Donor details included age, cause for death, any systemic or ocular disease or surgery. Donor tissue was examined in detail under slit lamp. Other details recorded were time of enucleation, storage media used and duration from enucleation to keratoplsty. Only grade A donor corneas were used for all the cases in the study. **Grade A** Mild epithelial oedema present and thickness of cornea increased by 10%, **Grade B** Mild epithelial oedema present. Descemets folds (peripheral) present. Peripheral endothelial changes present. Corneal thickness increased by 10-25%. **Grade C** All above changes in moderate to severe degree. Increase in thickness by 50 to 100%, **Grade D** Cornea totally hazy and no details can be made-out of anterior chamber and other structures.

All cases were done under local anesthesia using a peribulbar block. Donor tissue was harvested before cutting the recipient cornea. Graft host disparity was maintained at 0.5mm. Four initial fixation 8/0 sutures were at 12, 6, 3 and 9^{o} clock respectively. Interrupted 10/0 sutures were placed at the level of Descemets membrane along the circumference at the host graft junction. Follow-up was done daily for a week, then weekly for a month and subsequently monthly for a year. The factors assessed were visual acuity, graft clarity, IOP, signs of rejection of grafts, inflammation, uveitis , neovascularisation and wound integrity. The sutures were removed any time after 12 weeks if they were seen to contribute to graft neovascularisation, caused a significant amount of foreign body sensation and lacrimation postoperatively. Steroids were continued for an average of 06 months to 12 months unless the development of glaucoma prompted us to discontinue steroids. Topical 0.05% Cyclosporine was introduced in all cases to reduce the dosage of topical steroids.

III. Results

Study included 40 eyes of 40 patients, 30 male and 10 female. The youngest patient studied was 12 years and the oldest 80 years of age, with a mean of 50.85 years (SD – 18.35). Highest number 15 (37.5%) of patients were in the age group of 61-70 years.(TABLE 1)

Table 1 Demographic Profile

Age	Males	Females	Total	Frequency %
11-20	03	–	03	7.5
21-30	06	01	07	17.5
31-40	02	01	03	7.5
41-50	–	01	01	2.5
51-60	06	02	08	20
61-70	11	04	15	37.5
71-80	02	01	03	7.5

The most common indication seen for penetrating keratoplasty was Bullous Keratopathy (ABK/PBK) 13(32.5%) cases, followed by corneal opacity (post microbial keratitis scarring and post traumatic corneal scarring) 11(27.5%), repeat graft 03(7.5%) and traumatic corneal perforation 01(2.5%) case. The most common procedure done was PK alone 18(45%) cases, followed by 12(30%) cases of PK combined with cataract extraction and IOL implantation (triple procedure). 03(7.5%) cases of triple procedure with Glaucoma Drainage Device were also performed.(TABLE 2)

Table 2 Baseline Disease

Diagnosis	Males	Females	Total	Frequency %
ABK	4	3	7	17.5
PBK	4	2	6	15.0
Corneal opacity	9	2	11	27.5
Adherent leucoma	3	1	4	10.0
Microbial keratitis	4	1	5	12.5
Corneal dystrophy	2	1	3	7.5
Repeat graft	3	-	3	7.5
Traumatic corneal perforation	1	-	1	2.5

Secondary intervention after PK was done in a total of 03(7.5%) cases, the procedure performed were cataract extraction alone, glaucoma drainage device implant alone in 01 (2.5%%) cases each and both cataract

extraction with glaucoma drainage device in 01 (2.5%) case. The most common pre-existing ocular condition seen was vascularisation 08(20%) cases, followed by microbial keratitis 05(12.5%) cases and glaucoma 05(12.5%) cases. Follow-up at 02 weeks post operative period showed complications in 07(17.5%) cases. The common complications were penetrating keratoplasty glaucoma (PKPG) 03(7.5%) cases, vascularisation 03(7.5%) cases and rejection in 01 (2.5%) case. At 12 weeks of follow-up the most common complication seen were vascularisation and infection 05(12.5%) cases each, followed by glaucoma in 04(10%) cases. The follow-up at 1 year showed glaucoma and vascularisation to be the most common complications seen in 15(37.5%) cases each. The storage media used was moist chamber in 16 (40%) and Mc-Carey Kaufman (MK) media in 24 (60%) of donor corneas. Of the preserved corneas 28 (70%) were transplanted before 24 hrs, 11 (27.5%) between 24-48 hrs and 01 (2.5%) between 48-96 hrs.

IV. Discussion

The success of corneal grafting in visual rehabilitation of the corneal blind in India depends on survival of the grafts. Understanding the causes of graft opacification may help reduce the risk of failure. Pseudophakic and aphakic bullous keratopathy was the most common indication for PK in our study with a frequency of 32.5%. This is similar to the prevalence in the USA of 30% [8] to 39% [9], higher than in Saudi Arabia (7.8%) [10] New Zealand of 17.9% [11] Sweden (21%) [9] and Taiwan (17.6%) [12]. Corneal opacity shares second position with 27.5%. This is considerably higher than in Europe and the USA, where it falls bellow 1%, and similar to the findings of Chen et al. 27.9% [12] and Al-Towerki of 19.8% [10] for corneal scars.

Penetrating keratoplasty alone was done in 18(45%) cases in our series. 12(30%) patients with pseudophakic and aphakic bullous keratopathy had a combined operation. This distribution of the procedures is similar to the data for Sweden [13], where 21% of the patients had triple procedures. In their series only 15% of the cases with bullous keratopathy needed additional procedures. In our series 05(12.5%) cases needed additional procedures in the form of GDD (7.5%) and Trab (5%), which is more or less similar to the above study.

The incidence of PKPG varies from 9-31% in the early postoperative period [14-16] and from 18-35% in the late postoperative period [17-19]. In our study we observed glaucoma during early postoperative (12 wks.) period in 04(10%) cases and during late postoperative period in 15(37.5%) cases, which corresponds well with the above studies. Preoperative glaucoma was seen in 05(12.5%) cases, which was a risk factor for development of glaucoma in early post operative period (at 12 wks,Odds Ratio-2.58). Goldberg et al. in 1981 [19] reported the incidence of increased IOP to be higher in patients with repeat grafts (45% in the early postoperative phase and 52% in the late postoperative phase).

Follow-up at 02 weeks revealed vascularization in 03(7.5%) cases, at 12 wks in 05(12.5%) cases and at one year vascularisation was seen in 15(37.5%) cases of opacified grafts. Majority of the cases of post-operative vascularisation were those which had corneal opacity (post traumatic and post infectious keratitis, 40% of all vascularised grafts) and regraft (13.3% of all vascularised corneal grafts) as the indication for penetrating keratoplasty. Vascularisation is an established and recognized risk factor for corneal graft rejection and failure [20,21]. Graft rejection episodes are common varying from 20% to 35% in the literature [22]. We observed 07(17.5%) cases of graft rejection in our study, which finally resulted in opaque grafts. One case was observed during early post-operative follow-up, which resulted in vascularisation of cornea followed by graft opacification. The lower frequency (2.5%) of rejection in our study can be attributed to more aggressive treatment with topical steroids post operatively. In most large eye care centres, repeat PKP is the second leading indication for corneal transplantation, accounting for a mean of approximately 18% (range, 6% to 41%) of cases performed [23-26]. In our study repeat corneal transplantation accounted for 03 (7.5%) cases of all cases performed. This was well within the range given in the literature [24-26]. Of the three cases one developed vascularisation, other developed glaucoma and third one developed rejection and vascularisation. Penetrating keratoplasty alone was done and no other surgical intervention was performed concurrently. (TABLE 3)

Table 3 Various factors observed during follow-up

Factor	02 wks Frequency %	12 wks Frequency %	01 Year Frequency %
Glaucoma	7.5	10.0	37.5
Vascularisation	7.5	12.5	37.5
Infection	-	12.5	20.0
Rejection	2.5	-	15.0

Of the 40 cases included in the study 16(40%) donor corneas were stored in Moist Chamber at 4^{o}C. 12(30%) of these donor corneas were transplanted within 24 hrs and 04(10%) corneas were transplanted

between 24-48 hrs. The remaining 24(60%) donor corneas were kept in Mc-Carey Kaufman Media of which 16(40%) were transplanted before 24 hrs, 07(17.5%) between 24-48 hrs and 01 at 96 hrs. A significant correlation exists between endothelial cell loss and storage time (P<0.001) [27]. MK media was found to be associated with better graft clarity (odds ratio 2.8,at 12 wks).

V. Conclusion

The major risk factors for graft opacification observed are increased IOP, vascularization, infection excluding endophthalmitis and immunological rejection.of which pre-existing glaucoma is a significant risk factor for post keratoplasty glaucoma, modification of which can improve graft survival and clarity .Uncontrolled IOP after PKP can result in graft failure and visual loss. IOP should be monitored on a regular basis after corneal transplantation. Uncontrolled IOPs should be treated aggressively. Any patient with preexisting glaucoma must be evaluated carefully prior to the corneal transplants. Patients with uncontrolled IOPs or patients with borderline IOP control on 2 or more medications may be treated with either mitomycin-C trabeculectomy or GDD surgery prior to or combined with the PK. PKPG not responding to medications should be treated surgically. Mc Carey Kaufman media has a positive association as compared to moist chamber for graft clarity. The group studied is small and there is a need to carry out such a study on a larger study group with randomisation.

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