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Original research

Outcome of therapeutic penetrating keratoplasty in advanced infectious keratitis

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Abstract

Purpose: This study aimed to evaluate the anatomical, therapeutic, and functional outcome of therapeutic penetrating keratoplasty (TPK) in terms of success and failure.

Methods: In this retrospective study 57 eyes of 57 patients were reviewed. They had undergone TPK from December 2012 to June 2017. Data analyzed included the baseline demographic features and characteristics, preoperative diagnosis, and postoperative outcomes. The baseline characteristics included age, gender, laterality, indications of TPK, lens status, size of the recipient, grade of the graft, organisms identified, preoperative best corrected visual acuity (BCVA), secondary procedures, adjunctive surgical procedure, postoperative BCVA at last follow-up, intraocular pressure (IOP), and long-term complications of TPK. The ultimate outcome of TPK was observed in terms of anatomical, therapeutic, and functional outcome which indicated the success and failure.

Results: A total of 57 eyes of 57 with an age range of 2–76-year-old patients who underwent TPK were included in the study. Perforated corneal ulcer was a major indication of TPK in 32 (56.1%) cases. Anatomical success was obtained overall in 49 (85.96%) cases. Indications of TPK and preoperative visual acuity, complications of TPK, and ultimate graft clarity showed significant impact on the anatomical outcome ($P = 0.03$, $P = 0.00$, $P = 0.00$, and $P = 0.05$), respectively. The therapeutic and functional success was observed in 51 (89.47%) and 40 (70.17%) cases, respectively.

Conclusions: Perforated corneal ulcers was the major indication for TPK. Indications and complications significantly affect the anatomical, therapeutic, and functional outcome.

Keywords: Therapeutic penetrating keratoplasty; Anatomical integrity; Therapeutic success

Introduction

It is estimated that 1.5 to 2 million new cases of corneal blindness are added annually due to ocular trauma and infective keratitis in developing countries which can be considered as a silent epidemic.[1,2] A national survey by the Government of India (1991–2001) estimated corneal pathologies constitutes 4% of all blindness. In India, more than 6 million people have unilateral corneal blindness with a vision of <20/200, whereas 1 million have bilateral corneal blindness. By 2020, >10 million people are expected to have corneal blindness.[3] Recently, corneal blindness has become a topic of global interest.[4]

Infective keratitis is a common vision-threatening entity which occurs in the whole world.[5] A significantly large proportion of eyes with microbial keratitis progress to corneal perforation,[6] resulting in severe ocular morbidities and even loss of globe.[7] Such cases often require an emergency surgical intervention, such as therapeutic penetrating keratoplasty (TPK). TPK can therefore help in saving many eyes

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structurally and functionally which otherwise may be lost.[8] TPK remains the most vital treatment strategy for perforated infectious corneal ulcers.[9] With improved economic development and access to medical care, the developing world is becoming better equipped to treat and cure infectious corneal ulcers.[10] In the developing world, successful outcomes of TPK for perforated infectious corneal ulcers have been reported in the literature.[11]

Maintenance of anatomical integrity of globe and eradication of the infective organisms are the primary goals of TPK, whereas visual rehabilitation is of secondary importance. Keeping that in view, this study was planned to evaluate the indications and outcome of TPK in terms of the anatomical integrity of the globe, therapeutic success, visual function preservation or visual gain, complications, and residual ocular morbidities in a tertiary institute of Uttarakhand.

Methods

The research was approved by the institutional research and ethical committee and was in accordance to the tenets set forth in the Declaration of Helsinki. A cross-sectional, descriptive study was conducted in which we retrospectively reviewed data of TPK's done from December 2012 to June 2017. The eyes of all the patients who underwent TPK and were operated by a single surgeon were included in the study to avoid surgical bias.

All the patients with perforated corneal ulcers, non-healing infectious corneal ulcers, molten grafts, or sloughed out grafts i.e. graft infection postoptical penetrating keratoplasty (post-OPK) or post-TPK and corneas with anterior staphyloma were included in the study.

Patients with a follow-up period of less than 18 months and corneal ulcers with associated endophthalmitis were excluded from the study.

Data analyzed included the baseline demographic features and characteristics, preoperative diagnosis and postoperative outcomes of TPK. The baseline characteristics included age, gender, laterality, indications of TPK, lens status, size of the recipient, grade of the graft, organisms identified, and preoperative best corrected visual acuity (BCVA). The postoperative outcomes were collected over a period of 18–24 months follow-up period, and they included eradication of infection, secondary procedures, adjunctive surgical procedure for enhancement of graft healing, like persistent epithelial defect in immediate postoperative follow-up, postoperative BCVA at last follow-up, intraocular pressure (IOP), and long-term complications of TPK. Corneal ulcers were considered central if located within 6 mm radius from central apex of cornea, and peripheral if any part of perforation was outside of this limit.[12]

Non-healing ulcers were those that were non-resolving after maximum medical therapy till one month.

The ultimate outcome of TPK was observed in terms of anatomical, therapeutic, and functional outcome which indicated the success and failure.

Anatomical success was considered the restoration of tectonic integrity of globe, and phthisis bulbi was considered as anatomic failure.

Therapeutic success was defined as complete eradication of primary infection after keratoplasty with appropriate adjunctive medical therapy, with no recurrent infiltrates on the cornea or sclera, recurrent hypopyon or endothelial exudates or plaques, and posterior segment involvement as vitritis or endophthalmitis.[13]

Functional success[14] was considered preservation of visual function with BCVA ranging from perception of light (PL), accurate projection of rays (PR) to $\geq$20/40. Functional failure was in terms of lack of light or inaccurate light perception. The BCVA <6/60 was considered as ambulatory vision.

In situ, corneoscleral rim excision was done for all eye donations, and donor tissue was collected in Mc Carey–Kaufman (M–K) medium with all aseptic precautions. Tissues were graded by grading chart by National Eye Bank as Grade A, B+, B, B−, C, and D. According to the National Eye Bank, grading donor cornea of Grade B or less can be used for TPK.[15]

There are fewer chances of graft re-infection, and it is easier to monitor the anterior chamber (AC) reaction in postoperative period with the use of healthy, clear, and good grade donor cornea. In these cases, severe inflammation and eventual elevated IOP are strongly anticipated, so graft with healthy endothelium can make the graft survive despite these factors. Therefore, in this study all the grades of cornea like A, B+, and B− were used for TPK depending upon the best available tissue at that time.

Surgical technique

Preoperatively intravenous mannitol was given in all cases to achieve hypotony. Most of the cases were done under general anesthesia.

Gentle trephination of the recipient bed was done up to 80%–85% of depth of recipient with an additional 1 mm rim of healthy corneal tissue for a stable and non-infected bed. Entry into AC was done with a 15-degree side port knife carefully and gently in perforated corneas. After putting viscoelastic from side port, cyclodialysis spatula was used to sweep the adherent and incarcerated iris from the site of perforation. Excision of recipient bed was done with Castroviejo's right and left corneal scissors. Excised recipient corneal tissue was sent for both microbiological and histopathological investigations after dividing into two parts. Special care was taken not to injure or touch the crystalline lens even if cataractous. Irrigation of AC was done with a balanced salt solution. Inflammatory membranes over iris and angles were peeled off gently. Angles were opened by sweeping with the iris repositor 360° and viscoelastic to keep the iris away from the peripheral cornea. The donor button was oversized by 0.5 mm which improve cooptation. In larger grafts involving limbus or sclera or aphakic recipients, a 1 mm larger donor grafts were taken. Sixteen or 24 interrupted sutures were applied depending upon the graft size with 10-0 nylon suture.

Viscoelastics and hyphema were washed off from the AC which was filled with air. Postoperative antimicrobials and antifungals were started depending upon the microbiology reports along with cycloplegics, artificial tears, and anti-glaucoma, if required. Oral corticosteroids were started in those cases where no evidence of fungal or gram negative organisms microbiologically existed.

Statistical analysis

Initially, data obtained were entered into an excel spreadsheet and then transferred to SPSS software (Statistical Package for Social Sciences, version 22, SPSS Inc, Chicago, IL) for analysis. Statistical data were expressed in terms of means ± standard deviations (mean ± SD). The descriptive statistics was used to express data in terms of frequency and percentage. Pearson Chi-square test (Fisher exact test) was used to find out the association between categorical variables and outcome (anatomical, therapeutic and functional) of TPK and all the tests were 2-tailed. P value < 0.05 was considered statistically significant.

Results

A total of 57 eyes of 57 patients who underwent TPK were included in the study. The age of the analyzed patients ranged between 2 and 76 years with mean ± SD of 49.58 ± 17.06 years. Among the patients, 41 (71.9%) were male.

Characteristics of keratitis

Indication of TPK was perforated corneal ulcer in 32 (56.1%) cases. The mean size of the perforation was 6.60 ± 1.11 mm, whereas the mean corneal ulcer size was 7.19 ± 2.13 mm. All patients were from rural areas. Mean follow-up of the patients was 13 ± 4.7 months. B-grade graft and graft size >8 mm were used in maximum cases 33 (57.9%) and 40 (70.17%), respectively. The organisms identified in maximum cases were fungal 11 (19.3%) and pathology was eradicated in maximum cases 47 (82.5%). Post-TPK the epithelial defect required adjunctive measures like tarsorrhaphy and amniotic membrane transplant for healing of epithelial defects in 11 (19.3%) each. Graft failure was seen in 30 (52.6%) cases. Seventeen (29.8%) patients underwent OPK as secondary procedure (Table 1).

Table 1
Summarized recipient related data.

Various variables	N (%)
Indications of TPK	
Perforated corneal ulcer	32 (56.1)
Non-healing corneal ulcer	14 (24.6)
Graft infection	9 (15.8)
Pseudocornea with anterior staphyloma	2 (3.5)
Lens status	
Phakic	41 (71.9)
Pseudophakic	12 (21.1)
Aphakic	4 (7)
Grade of graft	
A	2 (3.5)
B+	6 (10.5)
B−	33 (57.9)
Glycerine preserved cornea	16 (28.1)
Graft size (mm)	
≤8	17 (29.8)
>8	40 (70.17)
Graft clarity	
1	27 (47.36)
2	8 (14.03)
3	7 (12.28)
4	15 (26.31)
Organisms	
None	40 (70.2)
Fungal	11 (19.3)
Grams positive bacilli	5 (8.8)
Viral	1 (1.8)
Pathology eradication	
Yes	47 (82.5)
No	10 (17.5)
Adjunct for healing PED post-TPK	
Tarsorrhaphy	11 (19.3)
Amniotic membrane transplant	11 (19.3)
None	35 (64.8)
Complications	
Glaucoma	3 (5.3)
Graft failure	30 (52.6)
Cataract	3 (5.3)
Graft infection	6 (10.5)
Phthisis bulbi	8 (14.0)
None	7 (12.3)
Secondary procedure	
OPK	17 (29.8)
Trabeculectomy + MMC + RS	2 (3.5)
Cataract surgery	3 (5.3)
Repeat TPK	5 (8.8)
Evisceration	1 (1.8)
Triple procedure	2 (3.5)
None	27 (47.4)
Final BCVA	
<20/200	35 (61.40)
20/200–20/40	20 (35.08)
≥20/40	2 (3.5)
Anatomical outcome of TPK	
Anatomical success	49 (85.96)
Anatomic failure	8 (14.03)
Therapeutic outcome of TPK	
Therapeutic success	51 (89.47)
Therapeutic failure	6 (10.52)
Functional outcome of TPK	
Functional success	40 (70.17)
Functional failure	17 (29.82)

TPK: Therapeutic penetrating keratoplasty; PED: Persistent epithelial defect; BCVA: Best corrected visual acuity; OPK: Optical penetrating keratoplasty; MMC + RS: Mitomycin C with releasable suture.

Complications

All cases of post-keratoplasty glaucoma, graft infection, and cataract were seen in cases with graft size >8 mm. Thirty (52.6%) eyes showed graft failure as a complication of TPK. Graft infection was seen in 6 (10.5%) cases out of which 5 (8.8%) underwent re-TPK (Table 1). Secondary procedures and grade of the used graft influenced the complications significantly $P = 0.00$, $P = 0.05$, respectively.

Final outcome of TPK

Anatomical outcome of TPK

Anatomical success was maintenance of ocular integrity in 49 (85.96%) cases, but 8 (14.03%) cases failed and could not restore the integrity and become phthisical.

Preoperative diagnosis or indications of TPK and preoperative visual acuity showed significant impact on the anatomical outcome with $P = 0.03$, $P = 0.00$, respectively (Table 2). Postoperative factors like complications of TPK, ultimate graft clarity showed significant relationship with the anatomical outcome of TPK with $P = 0.00$, $P = 0.05$, respectively (Table 3).

Therapeutic outcome of TPK

Therapeutic success was observed in 52 (91.22%) cases, but in 6 (10.52%) cases, graft infection was seen, out of which 5 (8.8%) underwent re-TPK. One case developed panophthalmitis, and evisceration was done.

Functional outcome of TPK

Functional success was seen in 40 (70.17%) cases with 22 (38.59%) cases showed BCVA in range of 20/200–≥20/40 which was considered as ambulatory vision. Seventeen (29.82%) cases showed functional failure in terms of lack of light perception or inaccurate projection of rays out of which 8 (14.03%) cases went into phthisis. Adjuncts for healing, secondary procedures, complications, graft clarity, and final BCVA influenced the functional outcome in significant manner with P value 0.00 in all cases (Table 3).

Discussion

TPK helps in the removal of toxins and enzymes and eradicates the offending organism which leads to progression of keratitis. Cases with a large non-healing or perforated corneal ulcer (if not treated with TPK) can lead to severe complications like endophthalmitis, panophthalmitis, and loss of eye. Early intervention is mandatory to prevent such disastrous courses of the disease. Restoration of globe integrity and removal of the infective process are its primary goals, whereas visual rehabilitation is a secondary consideration.[3] Primary TPK is considered the most reasonable treatment option for large perforated corneal ulcers irrespective of the underlying etiology, although recently, alternative techniques such as using autologous fibrin membrane combined with solid platelet-rich plasma,[16] tenons patch grafts,[17] and partial thickness lamellar grafting techniques have been tried. In the present study, 71.9% of cases were males which is comparable to results by Prakash et al. with predominance of males (84.6%).[18] The trend of predominance of males for TPK in the developing world could be explained due to various socioeconomic factors and easy accessibility of the males to hospitals. Males are also more prone to trauma and corneal ulcers as compared to females. Although TPK was done mainly to

Table 2
Association of various pre- and intra-operative variables with the outcome of therapeutic penetrating keratoplasty (TPK).

Variables	Anatomical outcome			Therapeutic outcome			Functional outcome		
	Success	Failure	*P** value	Success	Failure	*P** value	Success	Failure	*P** value
Indications of TPK									
Perforated corneal ulcer	28	4		31	1		23	0	
Non healing corneal ulcer	13	1	0.034	11	3	0.037	13	1	0.00
Graft infection	8	1		8	1		4	5	
Pseudocornea with anterior staphyloma	0	2		1	1		0	2	
Preoperative visual acuity									
PR Inaccurate	0	1		1	0		0	1	
PL+, PR Accurate	37	6	0.00	37	6	0.39	29	14	0.14
CFCF	12	1		13	0		11	2	
Lens status									
Phakic	37	4		36	5		31	10	
Pseudophakic	10	2	0.078	12	0	0.31	8	4	0.10
Aphakic	2	2		3	1		1	3	
Grade of graft									
A	2	0		2	0		2	0	
B+	5	1	1.0	6	0	0.64	5	1	0.37
B−	28	5		28	5		20	13	
Glycerine preserved cornea	14	2		15	1		13	3	
Graft size (mm)									
≤8	14	3	0.68	15	2	1.0	12	5	1.0
>8	35	5		36	4		28	12	

*P** value calculated by Pearson Chi square test.
TPK: Therapeutic penetrating keratoplasty; PR: Projection of rays; PL: Perception of light; CFCF: Counting fingers close to face.

Table 3
Relationship of various postoperative variables with the outcome of therapeutic penetrating keratoplasty (TPK).

Variables	Anatomical outcome			Therapeutic outcome			Functional outcome		
	Success	Failure	*P*# value	Success	Failure	*P*# value	Success	Failure	*P*# value
Adjunct for healing post-TPK									
Tarsorrhaphy	10	1		10	1		10	1	
AMT	11	0	0.32	10	1	1.0	11	0	0.00
None	28	7		31	4		19	16	
Organisms									
None	34	6		37	3		28	12	
Fungal	9	2	1.0	8	3	0.46	7	4	0.92
Grams positive bacilli	5	0		5	0		4	1	
Viral	1	0		1	0		1	0	
Complications									
Glaucoma	3	0		3	0		2	1	
Graft failure	30	0		29	1		26	4	
Cataract	3	0	0.00	3	0	0.00	3	0	0.00
Graft infection	5	1		2	4		4	2	
Phthisis bulbi	1	7		7	1		0	8	
None	7	0		7	0		5	2	
Secondary procedure									
OPK	17	0		15	1		17	0	
Trabeculectomy + MMC + RS	2	0		2	0		2	0	
Cataract surgery	3	0		3	0		3	0	
Re-TPK	4	1	0.09	2	3	0.09	4	1	0.00
Evisceration	0	1		1	0		0	1	
Triple procedure	2	0		2	0		2	0	
None	21	6		25	2		12	15	
Graft clarity									
1	20	7		23	4		12	15	
2	7	1	0.07	7	1	0.36	6	2	0.00
3	7	0		6	1		7	0	
4	15	0		15	0		15	0	
Final BCVA									
<20/200	27	8		30	5		18	17	
20/200–20/40	20	0	0.05	19	1	0.52	20	0	0.00
≥20/40	2	0		2	0		2	0	

P# value calculated by Pearson Chi-square test.
TPK: Therapeutic penetrating keratoplasty; AMT: Amniotic membrane transplant; OPK: Optical penetrating keratoplasty; MMC + RS: Mitomycin C with releasable suture; BCVA: Best corrected visual acuity.

decrease the infection load, its secondary function was to improve the vision. Perforated corneal ulcer was a major (56.1%) indication for TPK in this study which is comparatively more than these reported cases of Sharma et al. (25.4%).[14] This can be explained by the fact that these patients were from rural backgrounds with negligible medical facilities. Indications of TPK affected the overall outcome (anatomical, therapeutic, and functional) in a significant manner. Anatomical success was seen in 85.96% of cases which is comparable to the results by Sharma and Sony et al.[14,19] BCVA >6/60 was seen in 38.59% of eyes which is lesser as compared to the western literature where it was reported between 50% and 80%.[20] There is a higher prevalence of risk factors for poor visual prognosis after TPK in patients of this current study such as history of ocular trauma with organic matter during agricultural work, delayed diagnosis, inappropriate management, lack of modern facilities in rural areas, and use of traditional or cocktail eye medications.[21] These factors lead to more perforations which lead to poor prognosis as perforated corneal ulcers were seen in 56.1% of all cases. A paucity of good quality donor tissue forces us to keep our criteria for donor tissue quality less stringent, more so in these emergency situations which lead to graft failure and fewer chances of functional success.

The ambulatory vision was achieved in 38.59% of cases which is consistent with 35.96% as reported by Sharma et al.[14]

Complications after TPK showed significant impact on the anatomical, therapeutic, and functional outcome. Secondary procedures and grading of the used graft affected the complications significantly. In this study, the majority of cases (52.6%) showed graft failure (rejection). It has been reported by Hill et al. that graft failure occurs in 14.6%–52.1% of cases after TPK.[8] Graft failure may be clinically difficult to differentiate with milder graft rejection episodes which was true for this study also. In this study incidence of glaucoma was 5.3% which is quite less as compared to 19.4% reported by Sony et al.[19] but comparable with 3.8% as reported by Prakash et al.[18] Therapeutic success was seen in 89.47% of cases which is comparable to the results reported by Sukhija et al. which was 90%.[22]

The other complications such as re-infection, persistent epithelial defect, and cataract were also more common in perforated ulcers and larger grafts.

A larger graft size >8 mm was associated with a lower visual outcome as compared with a smaller graft size in our study and has also been reported by Li et al.[23] This may be attributed to extensive and virulent initial infection, inappropriate and inadequate initial medical management, vascularization of the graft, delay in surgery, postoperative chronic ocular surface and anterior segment inflammation and secondary glaucoma.

The sample size is small, and the data is highly skewed. Variables are not normally distributed, so the regression analysis was not used for statistical analysis. The limitations of this retrospective study were that in over half of our cases, there was no inciting event, and in the majority of our cases, no infecting organism was identified. This could be explained because most of the cases referred to our tertiary eye care were recalcitrant, incompletely treated by cocktail therapies including topical antibiotics, antiviral and antifungal therapy at multiple centers. Furthermore, polymerase chain reaction (PCR) was not done for suspected herpetic infections, where it was not possible to identify the organism. Due to the paucity of fresh donors, cornea glycerine preserved corneas were also used which do not have viable endothelium and was therefore bound to make the graft failure mandatory which could have tilted the outcome. Specular endothelial cell count was not done for donor corneas.

In conclusion, TPK has a definitive role in the management of refractory keratitis with high anatomical, therapeutic, and functional success. Smaller graft size lead to fewer complications. The indications and complications of TPK affects the overall outcome of surgery.

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