Outcome of Therapeutic Penetrating Keratoplasty in infective keratitis at a Tertiary Eye Hospital

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Abstract
Objective: To find out the outcome of therapeutic keratoplasty in infective keratitis.
Methods: Medical records of patients, who underwent therapeutic keratoplasty from January 2017 to January 2018, were reviewed retrospectively. Data collected included demographic parameters, indications for surgery, microbiology of the ulcers and donor tissue details. In the follow-up period, ocular status was evaluated in terms of eradication of disease, anatomic success, graft clarity, visual acuity, and development of glaucoma and cataract.
Results: 90 eyes of 90 patients were enrolled in the study. Male and female ratio in present study was 3:2. Average age was 45.4±13.7 years. Overall, 71%( 64) of infective keratitis was perforated on presentation. A total of 51 (56.6%) eyes were positive for organisms of which 25 showed pure fungus, 24 showed pure bacteria and 2 showed mixed infection. The commonest fungus and bacteria isolated were Aspergillus and Streptococcus, respectively. Average follow-up period was 11±2.3 months. Overall cure rate of infection was 88.8%, anatomical success rate was 90%, and graft clarity was 36.6%. Overall, 43.3% had secondary glaucoma. In the postoperative course, 66.6% of phakic eyes had developed cataract. Overall functional success with a visual acuity above 6/60 was 25.5%. Bacterial keratitis had a significantly higher cure rate, anatomical success, and graft clarity compared to fungal keratitis.
Conclusion: Therapeutic keratoplasty is an important procedure to save the eye and preserve vision in severe infective keratitis. There is a high incidence of postoperative glaucoma, cataract, and graft failure in such a surgery. Bacterial keratitis has a better outcome than fungal keratitis.
Keywords: Therapeutic penetrating keratoplasty, Infective keratitis, Fungal keratitis.

Introduction
In developing countries, corneal ulcer is the major cause of visual impairment and blindness.1 Lack of accessibility of eye care, delayed or inappropriate treatment, and microbes not responding to antimicrobial therapy may result in a large or perforated ulcer which will necessitate therapeutic penetrating keratoplasty (TPK). The procedure is meant to terminate or reduce an actively infectious corneal disease or repair an anatomic defect in the cornea.2 It is generally performed in an emergency basis, and its primary goal is to reestablish globe integrity and to eliminate infection. Visual rehabilitation is a
secondary consideration. TPK constitutes a significant proportion of keratoplasty performed in Asian and other developing countries. TPK carries a risk of recurrence of infection and also has a higher risk of graft rejection and graft failure compared to optical keratoplasty. It has a higher incidence of postoperative uveitis, glaucoma, synechia, and cataract.

Materials and Methods
This is a retrospective study. Medical records of patients, who underwent therapeutic keratoplasty from January 2017 to January 2018, were reviewed. Data were collected about demographic parameters, indications for TPK, microbiology of the ulcers, details of donor tissue in terms of donor age, graft size, and endothelial density, duration of follow-up, and any significant events happening in the postoperative period. The outcome of TPK was measured in terms of anatomic stability, eradication of disease, visual acuity, graft clarity, and development of cataract and glaucoma. Comparison was made between the outcome of bacterial and fungal ulcer undergoing TPK. In those cases that had undergone TPK more than once, only the first TPK was considered for outcome assessment.

Surgical Procedure and Management
The TPK was performed under peribulbar block, except in children and patients presented with perforation. The criteria for quality of the donor tissue may not be as stringent as for optical penetrating keratoplasty. So, even very old, aged cornea or with low endothelial cell count was used. In all cases, the donor size was exceeded by 0.5 mm. The recipient cornea was incised using either a handheld or a vacuum trephine. Care was taken to avoid pressure on the globe. In case of a large perforation and sloughing ulcer, freehand dissection of the host bed was performed, after initial marking with a trephine. The entire infiltrated area along with 1 mm of healthy corneal tissue was removed in all the cases. The excised corneal specimen was sent for microbial investigations. Purulent material was irrigated from the anterior chamber (AC). Inflammatory membranes over the iris and pupil were mechanically removed with forceps. Anterior and posterior synechia were released. One or two iridectomies were performed to prevent pupillary block glaucoma. 10-0 Nylon interrupted sutures were used to close the graft host junction. Postoperatively, the duration of antimicrobial treatment as well as initiation and frequency of steroids were titrated based on severity of infection, type of infection, associated epithelial defect, and postoperative inflammation. Fungal keratitis requires longer treatment than bacterial. Steroids were started almost immediately in bacterial keratitis but in fungal, it was delayed by 1 to 2 weeks postoperatively. In case of recurrence of the infection, steroids were avoided. Other postoperative problems including formation of synechia, shallowing of AC, secondary glaucoma, nonhealing epithelial defect, and loose sutures were managed with supportive medications and/or with procedures such as AC reformation, suture removal, glue + BCL and resuturing of the wound.

Results
Overall, 90 eyes of 90 patients had undergone TPK for infective keratitis; 60% were male. Average age of the patients was 45.4±13.7 years. 3 patients had undergone TPK more than once in the same eye. Average waiting time of patients for TPK was 4.2±3.52 days. Average age of donor cornea and endothelial cell count was 65.5±17.1 years and 2,021.5±471.4 cells/mm2 respectively. Mean recipient rim size was 8.52±0.38 mm. A total of 64 cases (71%) were perforated corneal ulcers and the remaining were non-healing ulcers or ulcers impending to perforate. Out of 90 eyes of TPK, 51 (56.6%) were positive for organisms of which 25 showed pure fungus, 24 showed pure bacteria, and 2 showed mixed bacteria and fungus. (Table-1) 39 Culture-negative cases were treated according to the clinical diagnosis. All patients had undergone full thickness keratoplasty. Out of 90 TPK, 12 surgeries (13.3%) were...
combined with extracapsular cataract extraction without posterior chamber intraocular lens. Overall cure rate was 88.8%. Recurrence of infection occurred within 2 weeks in bacterial keratitis and within 1 month in fungal. All eyes with recurrence underwent second TPK. All second TPKs were successful in eradication of infection. (Tables 2) The average follow-up duration was 11±2.3 months. On follow-up of 60 eyes (66.6%) had documentation of variable grades of cataract. 39 cases (43.3%) had secondary glaucoma. 5 cases out of 39 cases of glaucoma needed interventional treatment in form of transscleral cyclophotocoagulation, valve implant and trabeculectomy.

**Table 1** Etiology of corneal ulcer

| Organisms                      | No. |
|-------------------------------|-----|
| Fungus                        | 25  |
| Aspergillus                   | 13  |
| Fusarium                      | 9   |
| Fungus (unspecified)          | 3   |
| Bacteria                      | 24  |
| Streptococcus pneumoniae      | 10  |
| Staphylococcus aureus         | 5   |
| Gram -ve rod (Pseudomon and Klebsiella) | 9   |
| Mixed ulcer (Fungus and Bacteria) | 2   |
| Culture-negative and unproven | 39  |

**Table 2** Recurrence of infection

| Type of infection          | Recurrence of infection | %  |
|----------------------------|-------------------------|----|
| Fungus                     | 7/25                    | 28 |
| Bacteria                   | 2/24                    | 8.3|
| Mixed                      | 0/2                     | 0  |
| Culture negative           | 4/39                    | 10.2|
| Total                      | 13/90                   | 9   |

**Discussion**

The mean age group of our patients, 45.4±13.7 years, is similar to that in Northern India, but varies with other Asian countries where the mean age was 55 years. Similar to our study, male preponderance of the patients is also seen in India, and Singapore. This could be because more men work outside home and are prone to work-related trauma. Corneal ulcers presenting to our Institute of are severe, already perforated, or impending to perforate. That is why 71% of TPKs were done for perforated corneal ulcers. Sedghipour et al, Sukhiha and Jain reported even greater proportion of perforated ulcers, 76%–88%. We had a large number of culture negative cases. This could be because patients were already treated with various antimicrobials before they came to us. In our study, the ratio of fungal to bacterial ulcers undergoing TPK was 1:0.96. In other studies done in Asia, this ratio ranges from 1:0.7 to 1.3:1.5. Similar to our study aspergillus is the commonest fungus needing TPK in North India but in Singapore, it is Fusarium. Recurrence of infection is a very undesirable complication which may again stake the structural integrity of the operated eye. Our study shows fungal ulcers undergoing TPK have higher chances of recurrence than bacterial ulcers (Table 2). Other reports mention recurrence rate of fungus after TPK to be 7.3%–10%. Our high recurrence rate of 26% could be because of residual infection in the recipient rim and because many fungal corneal ulcers presenting in our institute were advanced with extensive invasion of anterior segment structures. Sharma et al quoted the cure rate of bacterial ulcers as 90%–100% and our bacterial cure rate also lies within this range. In our study, overall anatomic stability after primary TPK was 90% (Table 3), which is similar to that reported by Cristol et al and Sukhiha and Jain. Anatomic stability was more in TPK performed for bacterial ulcers than for fungal ulcers. Sharma et al and Chen et al reported 90%–92% anatomical success rate for bacterial and 84.6%–88.5% for fungal ulcer. Graft clarity was less in the case of fungal than bacterial ulcers, (Table 3). Sharma et al mentioned that the range of clear graft at 1-year follow-up varied from 69%–100% in bacterial ulcers and varied from 51%–84% in fungal ulcers. In our study, with an average follow-up period of 11 months, graft clarity was 36.6%. The majority of patients was from far rural areas and did not regularly follow up, and this had an implication in the graft survival. In total, 25.5% had a visual acuity above 6/60 after achieving anatomic success. Sharma et al reported 14.8% patients with a visual acuity above 6/60 at 1-year follow-up. Cataract is a common complication of
corneal ulcer, surgical procedure, inflammation, and topical steroids. In our study, presence of cataract in phakic TPK eyes was 66.6%. There is reporting of 51%–77.7% incidence of cataract in TPK done for active viral keratitis. Secondary glaucoma is mostly due to extensive peripheral anterior synechia and may lead to graft failure and blind eye. We noted a high incidence of secondary glaucoma of 43.3% compared to that reported by Sharma et al and Sukhija and Jain who mentioned 25% and 22%, respectively.

Table 3 Anatomic stability and Graft clarity

| Type of infection | Anatomic stability | Clear graft |
|-------------------|--------------------|-------------|
| Fungus            | 20/25              | 5/25        |
| Bacteria          | 23/24              | 11/24       |
| Mixed             | 2/2                | 1/2         |
| Culture negative  | 36/39              | 16/39       |
| Total             | 81/90              | 33/90       |

Conclusion

Therapeutic keratoplasty has a definite role in the management of perforated and/or severe infective keratitis. TPK provides structural stability, ambulatory vision, and can preserve potentiality of vision. Presence of infection and inflammatory status of the eye at the time of TPK makes the postoperative course challenging. Bacterial ulcers undergoing TPK have a better outcome in comparison to fungal ulcers.

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