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Therapeutic Penetrating Keratoplasty: Indications and Surgical Outcome

Dr priyanka sankhla

SNMC jodhpur

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I. Introduction

Serious corneal disorders like ulcers or perforations frequently give rise to difficult clinical situations, with rapid consecutive threatening of vision and disintegrity of the eye globe. Despite current advances in pharmacological and surgical treatment, severe corneal infections, injuries, or systemic diseases can lead to corneal perforations, which frequently require surgery. Corneal ulcer is the major cause of visual impairment and blindness indeveloping countries.[1]

Lack of accessibility to healthcare facilities, delayed treatment, and resistance to antimicrobial therapy lead to worsening of ulcer and even perforation which finally require a Therapeutic Penetrating Keratoplasty (TPK).

The procedure leads to replacement of infected tissue with a normal sterile donor corneal button.Its primary goal remain the eradication of infected tissue and reestablishment of globe integrity. The visual rehabilitation is of secondary consideration which may or may not be achieved. TPK constitutes a significant proportion of keratoplasty performed in Asian and other developing countries.[2]

TPK carries a risk of recurrence of infection and also has a higher risk of graft rejection and graft failure compared to optical keratoplasty. The postoperative complications such as uveitis, glaucoma, synechia, and cataract are higher as compare to optical penetrating keratoplasty. [3]

Urgent reconstructive surgical interventions may be necessary to avoid consecutive endophthalmitis and the formation of the anterior and posterior synechiae and secondary glaucoma and to prevent the spread of pathogens toward the posterior pole of the eye globe or to avoid other severe complications [4,5,6,7].

The study is done to find out the outcome of TPK. This will also be helpful in providing the information for further prospective studies. Also, we will be able to identify the risk factors for the graft failure changes that need to be done to improve the outcome.

II. MATERIALS AND METHOD

We retrospectively reviewed the outcomes of the surgical treatment of 35 patients that were operated on using the total penetrating keratoplasty technique. All surgeries were performed between september 1, 2015 and September 30, 2020.

Various parameters included in the study were demographic profile of patients, indications for surgery, microbiological status, donor tissue details and complications of the surgery. The results were assessed in terms of eradication of disease, anatomic success, graft clarity, visual acuity, and development of complications. Comparison was made between the outcome of bacterial and fungal ulcer undergoing TPK

SURGICAL TECHNIQUE AND POSTOPERATIVE MANAGEMENT

The TPK was performed under Local anesthesia in all patients after giving intravenous 20% mannitol 5ml/kg body weight half hour before surgery.

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 were used if better tissues were not available. In all cases, the donor size was exceeded by 0.5 mm the recipient size. The recipient cornea was incised using corneal trephine. Optimal graft size was determined by placing various-sized trephines on the recipient cornea to encompass the entire area of pathology. A 360-degree peritomy was performed at the limbus before trephination to facilitate suturing. The donor tissues (corneoscleral rings) were preserved in a cold storage media of Eusol-C solution (Alchimia, S.r.I., Ponte S. Nicolo, Italy). All surgeries were performed under general anaesthesia. To avoid consecutive glaucoma, all patients received peripheral iridectomy, unless an iridotomy or iridectomy had been performed during a preceding surgical intervention. For TPK, we used a

Hanna vacuum trephine system (Moria Inc., Antony, France) or freehand trephines, if globe integrity was seriously damaged. All grafts were sutured with single 10-0 nylon sutures into the recipient sclerocorneal bed; the knots were buried. Because of the high risk of rejection in large grafts, both topical and systemic steroid medication was administrated individually, postoperatively. Also, intensive topical and general medical management for the primary ocular pathology was continued, according to its aethiology: immunosuppression, anti-inflammatory, broad-spectrum antibiotic, and antifungal or antiprotozoal therapy, respectively. Patients were also treated with cycloplegics and antiglaucomatous medications, if necessary. Because of the complex nature of underlying pathology, additional one-time or subsequent surgery was performed more than once. We followed up with all patients every two weeks for a period of three months, monthly for a minimum of six months and at differing intervals, thereafter. The mean observation time was 24 months (from 1 to 60 months).

III. RESULTS

Forty-seven eyes of forty-six patients were operated on between September 1, 2015 and September 30, 2020, using the total penetrating keratoplasty technique. This group consisted of 21 females, whose mean age was 66.13 ± 9.94 (range 39 to 80 years), and 25 males, whose mean age was 63.69 ± 14.48 (range 32 to 92 years). There was no statistically significant difference with respect to gender and age between both groups ($p > 0.05$).

All primary causes of corneal destruction and perforation requiring TPK are presented in Table 1. The main cause of this condition was infection. The most frequent infectious factors were bacterial cultures (*Pseudomonas aeruginosa*: 3 eyes (14%); *Enterococcus faecalis*: 2 eyes (9%); *Escherichia coli*: 2 eyes (9%); *Proteus mirabilis*: 3 eyes (14%); *Staphylococcus aureus*: 2 eyes (9%); and *Staphylococcus epidermidis*: 1 eye (5%)) and fungal (*Aspergillus fumigatus*: 3 eyes (14%); *Fusarium solani*: 2 eyes (9%); and *Candida albicans*: 2 eyes (9%)). Autoimmune diseases involved rheumatoid arthritis (7 eyes: 70%), ankylosing spondylitis (2 eyes: 20%), and lupus (1 eye: 10%). Eye injuries were dominated by chemical, mainly alkali, burns of the ocular surface: 8 eyes (67%). Ocular complications of Lyell's syndrome involved 2 patients (2 eyes: 100%). Neurotrophic keratopathy (loss of the neurosensory innervations of the cornea) was responsible for corneal perforation in one eye.

Table 1- Causes of the corneal tissue destruction and perforation

Cause of perforation	**Total (*n* =47) 100%**	**Female (*n* = 22) 47%**	**Male (*n* = 25) 53%**
Bacterial infection	13(27.6%)	6(10.6%)	7(17%)
Fungal infection	7(14.9%)	4(8.5%)	3(6.3%)
Protozoal infection	2(4.25%)	1(2.1%)	1(2.1%)
Autoimmune diseases	10 (21.3%)	6 (12.8%)	4 (8.5%)
Chemical injury	8 (17%)	3 (6.3%)	5 (10.6%)
Penetrating injury	4 (8.5%)	1 (2.1%)	3 (6.3%)
Others	3 (6.3%)	1 (2.1 %)	2 (4.25%)

The main cause of surgical treatment failure was persistent epithelial defect, observed in 34 operated eyes (72%), resulting from decreased corneal sensitivity and impaired tear production. There were 22 eyes (65%) with persistent epithelial defect refractory to medical therapy, with consecutive ulceration and perforation of the cornea requiring subsequent tectonic surgery. Repeated total penetrating keratoplasty, penetrating keratoplasty, or corneoscleral patch graft was performed on 11 eyes, including 2 eyes of 2 patients where the tectonic approach was necessary more than twice, as were the eyes of patients with Lyell's syndrome. In one eye of a patient with Lyell's syndrome, despite successive surgical approaches, eyeball atrophy occurred.

Reinfection was observed in 19 (40%) of eyes that received TPK surgery. Despite vigorous antimicrobial topical and general treatment and repeat tectonic surgery (3 penetrating keratoplasties, 2 total penetrating keratoplasties, and 1 corneoscleral patch graft), 11 (58%) of reinfected eyes developed endophthalmitis, which demanded the radical surgical approach of evisceration. Three eyes developed phthisis.

Graft melting, reported in 16 eyes (34%) and frequently preceded by loosening of the sutures and tissue necrosis resulting from infection or immunological mechanisms, was another important complication of TPK. Primary surgical treatment failed in 12 eyes (25%), and successive surgical treatment was performed: repetitive

TPK in 8 eyes and CSPG in 4 eyes. Of this group, 5 eyes (31%) experienced complications from infection, 3 eyes developed phthisis, and evisceration was necessary in 2 eyes.

Early graft rejection, characterised by a whitish, sterile ring or diffuse infiltrates, was present in 5 eyes (11%) and treated for infectious corneal ulcerations. Intensive topical and systemic immunosuppressive and anti-inflammatory treatment was administered, leading to scarring and thinning of the perilimbal tissue. No urgent surgical approach was necessary.

Subsequent consecutive glaucoma or ocular hypertension occurred despite surgically performed iridectomy during tectonic TPK. Peripheral iridectomy was reported in 15 eyes (32%). To normalize refractory to medical treatment in intraocular pressure, 10 eyes (67%) required surgical intervention: 5 trabeculectomies, 3 transscleral cyclophotocoagulation, and 2 Ex-press glaucoma shunt implantations.

Table -2 Postoperative complications of total penetrating keratoplasty

Complication rate	**Primary cause of ocular disease**	**Infections**	**Autoimmune diseases**	**Trauma**	**Others**
Persistent epithelial defect		13 (59.1%)	9 (90%)	9 (75%)	3(100%)
Reinfection		15 (68.2%)	3 (30%)	1 (8.3 %)	0
Graft melting		8 (36.4%)	7 (70 %)	2(16.7 %)	0
Graft rejection		5(100%)	0	0	0
Glaucoma or ocular hypertension		4 (18.2%)	4 (40%)	6 (50%)	1 (33.3%)

IV. DISCUSSION

The main purpose of tectonic surgery is restoration and maintenance of ocular integrity. Postoperative visual acuity and graft clarity are related to many complex immunological and physiological conditions. Anatomical integrity of the globe does not guarantee improvement of vision.

In our study, we assessed, like other authors[8,9] that the most frequent indication for rapid tectonic treatment was infection. However, despite maximum broad-spectrum medical and surgical multistage treatment, even when repeated, the final outcome remained frequently unsatisfactory and was considered a therapeutic failure. Endophthalmitis refractory to antimicrobial and anti-inflammatory treatment required the final procedure of evisceration[6,10].

Large grafts often are regarded as a risk factor for immunologic graft failure[11]. Our results agree with those reported by Ti et al.[10] and Jonas et al.[12]. Corneal graft melting, frequently observed in autoimmune disorders complicated by corneal perforations and usually preceded by loosening of the sutures, is also comparable in frequency, according to the foregoing author's reports.

Delayed epithelialisation or persistent epithelial defect determined a significant graft failure rate and contributed to the higher rate of ocular surface complications[6]. The final result of this complication often leads to repeated tectonic and reconstructive surgery [7,11,13].

In conclusion, total penetrating keratoplasties, despite the high risk of intra- and postoperative severe complications, constitute a true surgical treatment alternative method for large peripheral cornea and adjacent sclera perforations. Further investigation and development of new surgical techniques are necessary to improve the final results of corneal perforation treatment. The goal should be not only restoration of ocular integrity but also improvement of visual functioning.

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