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Ophthalmology

PROFILE AND OUTCOME OF URGENT THERAPEUTIC PENETRATING KERATOPLASTY AMONG PATIENTS WITH PERFORATED ADVANCED INFECTIOUS KERATITIS IN A TEACHING HOSPITAL OF KARNATAKA

KEY WORDS: corneal ulcer, keratitis, corneal transplantation, keratoplasty

Dr Khadeeja Shadin* Postgraduate, Dept Of Ophthalmology, Yenepoya Medical College, Mangalore. *Corresponding Author

Dr Rashmi Shambhu Assistant Professor, Dept Of Ophthalmology, Yenepoya Medical College, Mangalore.

Dr Rashmi Jain Associate Professor, Dept Of Ophthalmology, Yenepoya Medical College, Mangalore.

Dr Vidya Hegde Professor And HOD, Dept Of ophthalmology, Yenepoya Medical College, Mangalore.

Dr Anupama Bappal Associate Professor, Dept Of Ophthalmology, Yenepoya Medical College, Mangalore.

ABSTRACT

BACKGROUND: Therapeutic penetrating keratoplasty is the penultimate procedure for corneal ulcers refractory to medical management. It is performed either in progressive corneal ulcer refractory to maximal antimicrobial therapy or when there is a large perforation that threatens ocular integrity. Maintenance of anatomical integrity of globe and eradication of the infective organisms are the primary goals of therapeutic keratoplsty whereas visual rehabilitation is of secondary importance. The objective of this study is to report the profile and outcome of patients with advanced and perforated corneal ulcers who underwent urgent therapeutic keratoplasties. **METHODS:** An analysis of case records of patients who underwent therapeutic keratoplasties in a medical college hospital of coastal Karnataka during two years, from January 2018 to December 2019 was conducted. The demographic details of ten patients, pre operative findings, course, management, surgical procedure, post operative follow up findings, outcomes and any complications were noted and described. **RESULTS:** Nine out of ten patients had trauma and seven out of ten patients had fungal etiology for corneal ulcers. All ulcers were perforated. After therapeutic keratoplasty, anatomical and therapeutic successes were achieved in nine out of ten eyes. Among these nine eyes, only four eyes maintained graft clarity and achieved functional success. Complications noted were recurrence of infection, glaucoma, inflammation, and cataract. The challenges faced were inability in using steroids to control inflammation and compulsion to use of therapeutic grade cornea in certain situation. **CONCLUSIONS:** Penetrating keratoplasty is a useful procedure and should be tried even in advanced corneal ulcers as it helps preserve integrity of globe and to remove the infectious process. However, visual recovery remains only a secondary intention as in most cases complications compromise the graft clarity.

BACKGROUND

Infective keratitis can cause significant visual impairment, blindness, or even loss of the eye; thus potentially having a major impact on the individual. In India, studies from the past have highlighted its occurrence more frequently among men, those involved in agriculture, and more likely following trauma to the eye.[1] 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. Significantly large number of eyes with infective keratitis progress to corneal perforation, resulting in severe ocular morbidity and even loss of globe. Such cases often require an emergency surgical intervention like therapeutic penetrating keratoplasty.[2]

Therapeutic keratoplasty is the last option for managing advanced infectious keratitis which is non-responsive to medical treatment. It is performed either in progressive corneal ulcer refractory to maximal antimicrobial therapy or when there is a large perforation that threatens ocular integrity.[3] It also remains the most vital strategy for perforated corneal ulcers and helps in saving many eyes structurally and functionally which otherwise may be lost. Successful outcomes with this procedure have been reported in the literature. Maintenance of anatomical integrity of globe and eradication of the infective organisms are the primary goals of therapeutic keratoplsty whereas visual rehabilitation is of secondary importance.[2]

The present study was conducted with the objectives to describe the profile of patients who underwent therapeutic keratoplasty, to identify the indications and surgical interventions in the study group and to explain the post operative course and outcome in the operated patients.

METHODS

This study is an analysis of case records of ten patients who underwent therapeutic keratoplasties in a medical college hospital during two years, from January 2018 to December 2019. Clearance from institutional ethics committee was obtained (letter number YEC2/525 dated 21.11.2020) before collecting the data. Patients with advanced infectious keratitis and perforation, who underwent therapeutic keratoplsty for therapeutic or tectonic indications, were included in this study. Patients who underwent optical keratoplasty and those with infectious keratitis and perforation who were managed with modalities other than therapeutic keratoplsty were excluded.

The list of patients was retrieved from the register of eye bank and keratoplasty centre of the hospital. Later the details of the patients were obtained from the hospital medical record systems and the demographic details of the patient, pre operative findings, course, management, surgical procedure, post operative follow up findings, outcome and any complications were noted. The data was tabulated in Microsoft excel sheet and analysed.

For the final outcome , 'anatomical success' was defined as restoration of tectonic integrity of the globe, 'therapeutic success' was defined as complete eradication of the infection after keratoplasty and 'functional success' was defined as preservation vision more than perception of light in the eye, on follow up at three months.[2]

RESULTS

Ten eyes of ten patients who presented with severe, advanced and perforated infectious keratitis refractory to medical management and underwent urgent therapeutic keratoplasty during the study period were included for the analysis.

The demographic details, preoperative characteristics and outcome of the patients are summarized in **table 1**. All were adults except for a five year old child. There was male preponderance among patients. Fungal ulcer following trauma was most commonly seen. One patient had dengue encephalopathy and developed exposure keratitis when she was admitted in the intensive care unit. Five male patients were smokers and one of them (patient 4) was dependent on alcohol. The patients presented late, some of them after a month of onset of initial symptoms with multiple visits to doctors at different places and not being very compliant with treatment or follow up.

All patients had corneal ulcer involving full thickness of the cornea. The size of the ulcer was more than 4 mm in all cases and involving almost full cornea in half of the cases. Patient number 7 had already undergone keratoplasty some years back; he developed ulcer in the corneal graft area following a minor trauma. In all cases, vision in the affected eye was less than hand movements close to face and only perception of light was present. All corneal ulcers were perforated. The patients were receiving appropriate medical management in the form of antifungals, antibiotics and cycloplegics prior to surgical intervention.

These patients underwent therapeutic keratoplasty (standard full thickness corneal transplantation). The surgical procedure was performed under general anaesthesia or peribulbar anaesthesia. McCarey–Kaufman medium or Cornisol medium preserved donor corneas were used. Disposable hand-held corneal trephines were used for dissection of host cornea to cover the infiltrate edge of the ulcer completely. A freehand dissection of the host bed was done in case of large irregular perforations involving total cornea. The size of the graft depended on the size of the ulcer; the donor button was oversized by 0.5 to 1.0 mm and punched from the endothelial side. Excised host cornea was sent for microbiological and histopathological examination. The anterior chamber was irrigated to remove infective debris. Along with therapeutic keratoplasty, additional surgical procedures including cataract surgery with or without intraocular lens implantation, intracameral and intravitreal antibiotics and antifungals, anterior vitrectomy, peripheral iridectomy were done as indicated. The donor button was sutured using 16 interrupted sutures using 10-0 monofilament nylon material. Postoperatively, patients were prescribed oral and topical antibiotics and topical steroids in cases of bacterial keratitis. Oral and topical antifungals were given but topical steroids were withheld in cases fungal keratitis.

Patient 5 had extension beyond the limbus involving sclera and so he underwent sclerokeratoplasty. Patient 8 had endophthalmitis; hence he received intravitreal antibiotics, antifungals and vitrectomy in addition to keratoplasty. In half of the patients, lens removal was done.

Postoperatively anatomical and therapeutic success was achieved in nine out of ten eyes. One eye developed recurrence of infection and had to be eventually eviscerated (patient 5 – sclerokeratoplsty had been performed in this case as it had extension of severe fungal infection to limbus and sclera). Among these nine eyes, only four eyes maintained graft clarity and achieved functional (visual) success. Complications noted were recurrence of infection (two cases, one of which was medically controlled), graft ectasia due to uncontrolled intra ocular pressure (one case), intraocular inflammation (three cases), cataract (one case).The challenges faced were inability to use steroids to control inflammation and compulsion to use of therapeutic grade cornea in certain situations.

Table 1. Demographic details, preoperative characteristics and outcome of the patients who underwent therapeutic penetrating keratoplasty for perforated advanced infectious keratitis in a teaching hospital of Karnataka, 2018-19

Patient number	Age in years	Gender	Involved eye	Cause of the corneal ulcer	Causative agent	Anatomical and therapeutic success	Functional success
1	24	Male	Left	Trauma	Fungal	Yes	No
2	28	Female	Right	Exposure keratitis	Bacterial	Yes	No
3	35	Male	Left	Trauma	Fungal	Yes	No
4	45	Male	Right	Trauma	Fungal	Yes	No
5	58	Male	Right	Trauma	Fungal	No	No
6	5	Male	Right	Trauma	Fungal	Yes	Yes
7	43	Male	Right	Trauma	Fungal	Yes	Yes
8	40	Male	Right	Trauma	Not identified	Yes	Yes
9	60	Female	Left	Trauma	Not identified	Yes	Yes
10	70	Female	Left	Trauma	Fungal	Yes	No

DISCUSSION

Infectious keratitis usually affects people of working age group which can cause a significant financial burden in terms of lost wages and medical expenses. A significant proportion of these ulcers fail to respond to medical treatment and eventually require therapeutic keratoplasty. Commonly reported risk factors for failure of medical therapy include large ulcer size, presence of hypopyon, and the virulence of the infecting organism. Other factors such as delay in seeking treatment, financial problems, lack of access and non-compliance to treatment regimen may all play a role in the failure of medical treatment in resource poor settings.[4] In our study too, we noted that the patients presented very late and were not very compliant with treatment and follow up.

Therapeutic keratoplasty has a definitive role in the management of progressive infectious keratitis refractory to medical treatment. The primary aim of the procedure is to re establish the integrity of the globe and to eliminate the infectious disease process. Visual rehabilitation is a secondary outcome. Visual outcome depends on various factors such as the causative agent, timing of surgery, degree of inflammation, type of donor material used, and size of the graft used. For example, larger grafts have a higher incidence of graft rejection and failure compared to smaller grafts. Therapeutic keratoplasty is a challenging procedure and is associated with a poor prognosis for graft survival as compared with the optical grafts.[5,6]

A study from Northern India showed that eyes with smaller grafts had better anatomical and visual outcomes compared with eyes with larger grafts. A higher incidence of secondary glaucoma was seen in eyes with perforated ulcers than in eyes without perforation and in eyes with larger graft sizes than in eyes with smaller graft sizes. Better outcomes may be achieved with early intervention before perforation or limbal and scleral extension.[7] In our study, all the eyes were perforated and one eye had limbal and scleral extension which led to poor outcome.

Perforated corneal ulcers are the major indication for

therapeutic keratoplasty. Increased severity of the ulcer at presentation is associated with unfavourable outcomes. Complications increase with the larger size of the grafts.[2] There are higher chances of postoperative glaucoma, cataract, and graft failure in such a surgery.[8] Among our patients, one eye had glaucoma, one eye had cataract and six eyes had graft failure.

A study from tertiary care centre found that therapeutic keratoplasty was a difficult surgery to perform, especially when done in an acutely inflamed eye, and a number of complications were expected. The study noted a high incidence of secondary glaucoma, which was more common in perforated ulcers and in larger grafts than in nonperforated ulcers and in smaller grafts. A higher incidence of reinfection in the larger grafts was responsible for a greater anatomical failure as compared with that in the smaller grafts. The other complications such as reinfection, endophthalmitis, persistent epithelial defect, anterior synechiae, and cataract were also more common in perforated ulcers and larger grafts. These may be on account of a more complicated surgery in perforated and larger ulcers with high chances of incomplete excision of the infiltrated edges. Further, there is a frequent protrusion of the lens–iris diaphragm during surgery and a high risk of angle damage with subsequent synechial closure.[7]

The procedure of therapeutic keratoplasty offers a microbiological higher cure rate in bacterial keratitis; but recurrence of infection remains a concern following fungal, viral and acanthamoeba keratitis.[5,6] Results are better in bacterial keratitis than fungal keratitis.[8,9] Recurrence of the primary infection after therapeutic keratoplsty is the single most important cause of failure in most of the cases. In a study which assessed factors responsible for the recurrence of infection, it was found that fungal etiology, retro-iris exudates, coexisting endophthalmitis, and larger grafts were susceptible to recurrence. Early surgery might mitigate most of these factors. Despite the risk of recurrence, this surgery remains an effective treatment in severe nonresponsive keratitis.[3]

A study describing the outcomes of therapeutic penetrating keratoplasty in fungal keratitis showed that larger infiltrate prior to therapeutic keratoplasty had much higher risk of recurrences. The primary goal of the surgery is to eradicate the infection. Visual rehabilitation in these eyes is a secondary goal as graft survival in the presence of active and severe infection is poor.[10] In our study, majority of the patients had fungal keratitis and two cases had recurrences.

Due to a mismatch between the supply and demand of donor corneas with healthy endothelium, many of these eyes may receive donor corneas with relatively poorer endothelial cell counts than those eyes operated for noninfective causes. As steroids cannot be started immediately in the initial days postoperatively, many end up having a poor visual outcomes due to eventual disorganization of the anterior segment and the angle structure, also there high risk of graft rejection and vascularisation.[10] Similar challenges were faced in our patients too visual outcome was poor as steroids could not be started and as donor cornea endothelial count were poor.

A paucity of good quality donor tissue forces ophthalmologists to keep the criteria for donor tissue quality less stringent, more so in these emergency situations which lead to graft failure and fewer chances of functional success. However the advantages of using good grade cornea would be that it would be easier to monitor the anterior chamber reaction in postoperative period. Also, in these cases, as severe inflammation and eventual elevated IOP are strongly anticipated, graft with healthy endothelium can make the graft survive despite these factors.[2]

A study from South India reported some of the risk factors associated with poor clinical outcomes in microbial keratitis as delayed presentations, use of improper medications, large size of the stromal infilterate, tobacco use, and involvement of posterior cornea, diabetes mellitus and blockage of tear duct. Patients reported their main reasons for delay in seeing an ophthalmologist as a lack of pain or reduced vision causing the patient to believe the eye problem was not serious, lack of availability of a person to escort the patient to the eye hospital , lack of finances for travel costs , other family, work, or travel commitments , and lack of knowledge of local eyecare services.[1] Another study found risk factors for poor visual prognosis after therapeutic keratoplasty 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. These factors lead to more perforations which lead to poor prognosis as perforated corneal ulcers were seen in more than half of all cases.[2] Hence there is a need to pay attention to these factors in case of a corneal ulcer.

Dsespite the current advances in antimicrobial therapy, the management of acute infectious keratitis remains a formidable challenge. Infectious causes are a common indication of penetrating keratoplasty. Because keratoplasty during the acute infectious period is acknowledged to have poorer survival compared with elective keratoplasty in noninflamed and uninfected eyes, indications remain stringent. Urgent keratoplasty generally is reserved for end-stage corneal infections or progressive lesions refractory to maximal medical therapy. Factors important in deciding timing of surgery and graft type include causative organism, extent of infiltration, and available level of skills and instrumentation.[9]

The study which evaluated the outcome of therapeutic keratoplasty among 28 patients with severe microbial keratitis who were advised evisceration concluded that every eye deserves a fair chance. In this study, evisceration was required in only two out of 28 cases. Hence primary evisceration needs to be best avoided in infections limited to anterior segment. This study excluded cases with endophthalmitis.[11] In our study, only one of the ten eyes ended up in evisceration. Another eye with endophthalmitis was not excluded and it was saved with surgical intervention.

CONCLUSIONS

Penetrating keratoplasty is a useful procedure and should be tried even in advanced corneal ulcers as it helps preserve integrity of globe and to remove the infectious process. However, visual recovery remains only a secondary intention as in most cases as complications compromise the graft clarity.

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