

Review Article

Pediatric Corneal Transplant Surgery: Challenges for Successful Outcome

Ashok Sharma¹, Rajan Sharma²

¹Dr Ashok Sharma's Cornea Centre, Chandigarh, India

²Cornea Fellow, Dr Ashok Sharma's Cornea Centre, Chandigarh, India

Visual rehabilitation of pediatric corneal blinds is a major challenge to corneal transplant surgeons. Penetrating keratoplasty (PKP) is the only way to restore vision and prevent irreversible blindness due to amblyopia in children. Performing penetrating corneal grafts in children poses difficulty in evaluation, technical difficulties during surgery and problems during follow-up. Younger children do not cooperate for proper slit-lamp examination and need to be examined under general anaesthesia. In addition, the complications encountered post PKP, including allograft rejection, post PKP astigmatism and post PKP glaucoma are more frequent in pediatric group as compared to adult recipients. Even after a successful graft, the child requires rigorous treatment for amblyopia. Parents need to be counseled before surgery and possible visual outcome and chances of obtaining clear graft should be discussed.

Indications of Penetrating Keratoplasty

Indications of PKP may be grouped into congenital corneal opacities and acquired corneal opacities. Among the congenital causes Peter's anomaly, congenital hereditary endothelial dystrophy (CHED), posterior polymorphous dystrophy, sclerocornea, dermoid and mucopolysaccharidosis are common indications for performing surgery (Fig.1a) (Dana et al, 1995; Kasmann-Kellner et al, 1999). Of the acquired causes, the main indications are traumatic corneal opacities, infectious keratitis, keratoconus, post cataract surgery corneal edema and non-penetrating corneal edema (Dana et al, 1995). Corneal edema due to endothelial cell decompensation in patients with buphthalmos has been successfully treated with PKP (Toker et al, 2003). In cases of traumatic corneal scars the visual outcome depends upon the extent of injury to the posterior segment. The occurrence of indirect optic nerve injury, choroidal rupture and retinal detachment may limit the visual prognosis after PKP. In developing countries, corneal opacities resulting from healed infective keratitis (bacterial, viral and fungal) constitute a major group of indications among the acquired causes (Fig.1c) (Dada et al, 1999). Corneal opacities following keratomalacia is another frequent indication in developing countries (Fig.1b) (Aasuri et al, 2000). Corneal opacities following eye

Commercial interest:

Financial interest:

Received: 21.08.2018

Accepted: 20.11.2018

Corresponding author

Dr. Ashok Sharma

Dr. Ashok Sharma's Cornea Centre

S.C.O.2463-2464, Level-2

Sector-22 C

CHADIGARH 160022

0172-5005982,9814528495

E-mail: ashok.cornea@gmail.com, asharmappgius@yahoo.com

injuries also need PKP (Fig. 1d). Although rare, chemical injuries result corneal opacity and limbal stem cell damage and may require limbal stem cell transplant or amniotic membrane graft before considering DALK or PKP (Fig. 2 a,b). Congenital corneal opacities are usually bilateral, whereas acquired corneal opacities are mostly unilateral.

Age at the time of PKP

Recent studies have shown that PKP in children should be performed at the earliest to prevent amblyopia. In neonates with congenital corneal opacities, PKP is advocated as soon as the child is fit for general anaesthesia. In case of acquired corneal opacities, the waiting period for surgery should be minimized. Children are always given priority over adults in case of a long waiting list. It is widely accepted that penetrating grafts in pediatric group should be performed at the earliest. But how “early” it should be, still remains a question unanswered. Neonates with unilateral corneal opacity may be undertaken for PKP at 2 months of age. While neonates with bilateral corneal opacities, first eye may be operated at 10 to 12 weeks of age and the second eye may be taken 6 to 8 weeks later. Contrary to the conventional rule in adults, (according to which we usually operate the eye with poor vision first) in neonates if bilateral surgery is required, we operate the eye with better potential first. This is done to decrease the chances of developing amblyopia in the better eye.

Immune system & PKP

Neonates due to immunological immaturity are less predisposed to graft rejection. The immune system in neonates develops very early in gestation and is fully developed by birth but it characteristically has dominance of T suppressor cells and qualitatively less functional B cells. It has been well documented that the anterior chamber is a privileged site for transplantation. This is mainly due to the

absence of blood vessels in the cornea and non access to lymphatic system. This makes antigen presentation, which is the part of the afferent limb of rejection, ineffective. Clinical studies have also shown that in neonates with isolated corneal opacities, corneal transplantation in the neonatal period resulted in better prognosis in terms of both graft clarity and vision improvement (Hestle & Oslin 1997). The success of these grafts has been attributed to both neonatal immune tolerance and clear visual axis during the most initial period of visual development. However, at 6 months of age, the immune system is fully developed and hyperactive. Thus corneal grafts performed at this age are at higher risk for developing graft rejection.

Evaluation of Infants or Neonates with Congenital Corneal Opacities

Detailed examination of infants and neonates with congenital corneal opacities is essential to plan treatment. The visual acuity must be ascertained. Response to light stimulus, fixation at light source and following of the movement of illuminated/light source are helpful. Responses should be observed carefully and should be demonstrated to the parents as well. Detailed personal history, obstetric history and family history in a child with congenital corneal opacity is recorded. Detailed ocular examination may not be possible in the consultation chamber as the neonates and infants will never be steady to allow detailed slit lamp bio-microscopy. This part of the examination is better performed under general anesthesia and we can get the detailed anterior segment examination, measurements of corneal diameters (both horizontal and vertical) and intraocular pressure readings as well. Details of corneal opacity, whether central or peripheral, localized or diffuse, are recorded. Peripheral corneal opacities occur in partial sclerocornea and peripheral corneal ulcers. Central corneal scars may occur in Peter’s anomaly. Perforated corneal ulcer may

require therapeutic penetrating graft. Direct and indirect ophthalmoscopy to visualize retina is performed and details of retina, macula and disc are recorded.

Investigations

Ultrasonography, A scan and B scan are performed to evaluate vitreous and retina status. In case of microphthalmia, there is always a possibility of associated intraocular anomalies. The ultrasound biomicroscopy (UBM) gives more details of intraocular pathologies. UBM is of special importance in patients with corneal opacity and associated glaucoma. Configuration of anterior chamber angle, details of angle structure and ciliary body are better delineated by UBM. In patients with anterior staphyloma, UBM may provide correct position of the iris and details of iris incarceration or iris adhesions. UBM has been of immense value in studying the structural alterations in pathological conditions including sclerocornea, Peter's anomaly, aniridia and ocular trauma. The status of lens and the integrity of the posterior capsule should be evaluated. In case the cataract is present, an additional surgical procedure of cataract extraction and post chamber IOL implantation along with penetrating keratoplasty should be performed.

Pediatric Keratoplasty Constraints

Pediatric PKP poses a challenge to corneal surgeons. The major constraints to perform corneal transplants in neonates include technical difficulties due to small eyes and positive posterior pressure. In severe cases of sclerocornea, the distinction between the sclera, limbus and cornea is obliterated and decision on the size of graft and centration are difficult. Low scleral rigidity causes extreme positive posterior pressure, resulting in anterior bulge of iris lens diaphragm and makes the surgery difficult (de Laage 2000). At times the positive pressure is extremely high and causes

extrusion of lens, loss of vitreous. Associated ocular abnormalities i.e. cataract, glaucoma and microphthalmia make the surgical procedure complicated and increase the operating time significantly. In the immediate post operative period, severe inflammatory response is encountered. Post surgery evaluation is difficult and most of the times, examination under general anaesthesia (GA) is needed. In case the surgery is delayed, immaturity of the visual system leads to amblyopia.

Preparation before Corneal Transplant Surgery

The aim of corneal surgeons is to attain clear visual axis and prevent amblyopia by performing corneal transplant at an early age. Corneal transplants may be performed early when the child is fit for GA and should be examined by a pediatrician as well. A child with corneal opacities may have associated eyelid and adnexal abnormalities. These abnormalities should be corrected first so that the graft surface is well protected following surgery. Raised intraocular pressure should be controlled and brought to normal range either with medical treatment or surgical (glaucoma filtering surgery/drainage device) intervention. Associated posterior segment anomalies, including retinal detachment or vitreous hemorrhage should be evaluated and treated.

Donor Tissue

For neonates and children, excellent grades of tissue from younger donors (between 4 to 30 years) is best suited and recommended. Cornea from eye donors younger than 4 years are relatively difficult to handle during surgery. Donor cornea from infants and very young children have steeper cornea and may result in increased corneal curvature of the graft (Palay et al, 1997; Koenig 1986). Due to this, unusually high myopia (upto 60 D) may occur following use of steeper donor cornea from young donors. This makes amblyopia treatment difficult. The

donor cornea for corneal transplants in children should have endothelial cell count close to 3000 cells/mm². In published data donor age, donor cell count and death to storage time did not affect grafts surgery. However, lesser time interval between death to corneal transplant surgery has been associated with better graft success.

Surgery

Extremely high positive posterior pressure is a major intra-operative problem encountered during corneal transplant surgery in Infants and neonates. Although it is impossible to eliminate the positive posterior pressure, however every effort should be made to limit it to minimum. In case of smaller palpebral aperture, lateral canthotomy reduces posterior pressure. Use of pre-op miotic drops or intra-cameral miotics may be useful to keep iris lens diaphragm behind. Anaesthetist may be required to keep the neonate at deeper plane of anaesthesia. A non-depolarising muscle relaxant (NDMR) eliminates the risk of movement and contraction of extraocular muscle. Keeping head at a higher level than feet (15 degree anti-Trendelenburg position) may be helpful. Anaesthetist may be requested to hyperventilate the child in case posterior pressure is extreme. Hyperventilation decreases posterior pressure and vitreous pressure by reducing the central venous pressure and choroidal venous blood volume.

Digital pressure or application of Honan's balloon is another good option to keep posterior pressure down. External pressure on the globe due to speculum should be kept minimum. Flieringa ring should be applied in every case. Pre placed mattress suture is helpful in securing the graft immediately and injecting visco elastic substance pushes the iris lens diaphragm behind (Parrish et al, 1988). The number of mattress sutures used may be 1 or 2 depending upon the requirement. These sutures if needed can also be applied after trephination

of host cornea. Use of 8-0 silk or monofilament to place cardinal sutures in case of extreme positive pressure is a good option to secure the graft. A cohesive viscoelastic substance i.e. healon GV or healon 5 may be used to keep positive posterior pressure down and allow suturing.

Surgical procedure should be completed in a shortest possible time. After punching the donor tissue all the instruments required for recipient trephination and donor button suturing should be kept ready. Neonates or infants may be given intravenous mannitol 20% (0.5 to 1.5 gm / KBW) to reduce the vitreous volume and thus decreasing the positive posterior pressure. At times the positive posterior pressure is extremely high and it may not be possible to suture the graft unless we reduce it. We routinely leave the recipient corneal button attached at 3 '0' clock position and do not excise it completely. We place donor button in the recipient opening and start suturing. After securing donor corneal button with 4 cardinal sutures we excise the host corneal button and continue suturing. This intact recipient cornea, in situation of extreme positive pressure is put back on the recipient opening. Few (4 to 8) cardinal sutures are applied and posterior pressure is reduced with intravenous Mannitol. Once intra-operative normalizes, recipient corneal button is removed and the donor button is sutured. We have found this simple method extremely useful in combating high posterior pressure during cornea triple procedure (Nirankari and Sharma, unpublished data). In case positive pressure is extreme and passing of 10 '0' nylon is difficult and it is not holding, it is wise to use 8 '0' nylon / silk suture and replace these sutures after the suturing in complete. Pars plana vitrectomy before trephination has been advocated to prevent posterior pressure for patients who are at higher risk for developing extreme positive posterior pressure during penetrating keratoplasty.

Size of the Graft

In a large multicentric study this average graft size was 7.1 mm diameter. Graft size may be determined according to the diameter of the host cornea. For a normal sized cornea (10.5 mm) 7.5 mm diameter graft should suffice. However in case of micro-ophthalmia/microcornea graft size may be decreased according to the diameter of the cornea. Small grafts are required in the smaller diameter corneas as placing a normal sized graft (7.5 mm) in these cases, brings host-graft junction very close to the limbus which may predispose the graft to allograft rejection and its failure. Use of small diameter grafts in otherwise normal cornea may have several disadvantages. This may result in higher astigmatism. With the use of small grafts, the number of viable endothelial cells decreases significantly. In case the graft size is reduced from the size 8 mm to 6 mm diameter the number of viable endothelial cells on the graft decreases by 44%. Thus smaller grafts will be predisposed to graft failure as the redistribution of endothelial cells will result in a low final cell count of the graft (well below 1000 per mm). It is advisable to use over sized donor corneal button (0.5 mm) routinely. In a study 1 mm over sizing for pediatric case has been advocated to decrease incidence of peripheral anterior synechia (Vajpayee et al, 1999).

Alternatives to Penetrating Keratoplasty

In corneal opacities partially obscuring the visual axis, gas permeable contact lenses may be tried. Majority of the patients suffering from opacities off visual axis resulting from traumatic corneal lacerations can be managed by fitting rigid gas permeable contact lenses (Smiddy et al, 1989). Most of the children are co-operative for fitting and further monitoring. Parents are usually apprehensive of gas permeable contact lenses. Majority of children learn quickly how to insert or take out rigid gas permeable contact lenses. They take care of contact lenses as per directions.

In case opacification is central and peripheral cornea is clearer one can evaluate the child for auto rotational keratoplasty (Bourne & Brubaker, 1978). The significant advantage is that the risk of allograft rejection is eliminated and chance of graft success is enhanced. However, post keratoplasty astigmatism and other problems of operating on neonates/infants remain unchanged.

In case corneal opacity is central and larger part of the inferior cornea is clearer, one can consider optical iridectomy (Miller et al, 1989). Optical iridectomy performed on the superior half of the iris do not serve any purpose as large part of it will be covered by the eyelids. Optical iridectomy is best performed in the lower-nasal quadrant however, one can opt for lower-temporal quadrant in case opacity is extending into lower-nasal quadrant. In our experience patients are not happy with an optical iridectomy. Most of the times it does not provide adequate vision to prevent amblyopia.

Infants and children with superficial corneal disease may be evaluated for superficial keratectomy. Most of the children suffering from pannus or conjunctivization due to partial limbal stem cell deficiency can be treated with superficial keratectomy. Once a dissection plane is reached, it is extremely easy to remove the superficial corneal tissue. Children suffering from vernal ulcer and plaque formation need epithelial debridement and plaque removal in addition to medical treatment. The objective should be to achieve smooth and transparent corneal surface. To promote epithelization, bandage contact lens may be applied. Children suffering from chemical eye injury and having conjunctivization due to partial limbal stem cell deficiency need superficial keratectomy with amniotic membrane transplant (Fig2a,b).

In case of partial thickness corneal opacities or in condition where endothelium is healthy, deep anterior lamellar keratoplasty (DALK) may be advised. In case of superficial corneal opacities

due to healed bacterial or fungal corneal ulcers, one should consider lamellar keratoplasty. Corneal endothelium is healthy in these cases. Depending upon the depth of involvement of cornea, one may choose to perform either anterior lamellar keratoplasty or deep anterior lamellar keratoplasty (Panda et al, 1999).

Advantages of DALK are that all the intra-operative problems including extreme positive posterior pressure, danger of extrusion of lens and difficulties of suturing may be avoided. In addition, risk of allograft rejection in DALK is significantly less as compared to penetrating keratoplasty as the host endothelium preserved and endothelial rejection is the most common cause of graft failure post PKP (Walls et al, 2002). Post DALK astigmatism is lower and visual rehabilitation is faster. These procedures may not be suitable for children with corneal opacities and deep corneal vascularization. Cornea has been documented as site of viral latency and recurrence may occur from corneal tissue alone. Limbal dermoids are best treated with DALK depending upon the level of involvement (Fig 2c,d). We have treated a child suffering from corneal scarring due to multiple intrastromal foreign bodies in the right eye following cracker injury by performing DALK (Fig 3a,b). We have also treated corneal perforation with anterior staphyloma by performing DALK (Fig 3c). In the last few years, the use of femtosecond laser has helped in introduction of a new technique, the femtosecond laser-assisted lamellar keratoplasty (FALK) (Shousha et al, 2011; Yoo et al, 2008). The anterior segment OCT is used to guide excision of the exact depth of the pathology and laser is used to cut an identicle lenticule from donor button. The advantages of this technique is a smoother interface and better surgical results.

Endothelial keratoplasty first reported in 2008 in children is involves replacement of host Descemet's membrane with the donor

membrane and its healthy endothelium. Descemet's stripping endothelial keratoplasty (DSAEK) has been reported successful in children suffering from pseudophakic corneal edema, congenital hereditary endothelial dystrophy, posterior polymorphous dystrophy, buphthalmos due to congenital glaucoma and failed grafts (Kymionis et al, 2012; Hashemi et al, 2012). DSAEK is more often considered and preferred as it avoids most problems faced following PKP. Some of these advantages include lower graft rejection, no suture related complications, minimum surgery induced astigmatism, fast visual rehabilitation and early amblyopia treatment. DSAEK also avoids intra-operative risks associated with "open-sky" technique. Descemet's scoring may be difficult in children. Because of this reason several surgeons advocate non Descemet's stripping automated endothelial keratoplasty (Anwar & El-Danasoury, 2014).

High Risk Penetrating Keratoplasty

Presence of deep corneal vascularization in two quadrants or more predisposes the corneal grafts to higher risk of allograft rejection. Children having undergone penetrating keratoplasty for herpes simplex keratitis are at higher risk of graft rejection, recurrence of disease and failure. Children should be put on oral acyclovir prophylaxis. In children having undergone regrafting, there is higher risk of allograft rejection due to prior sensitization. Patients having corneal opacities in association with limbal stem cell deficiency and ocular surface disease are also at higher risk of developing graft failure due to allograft rejection. In such cases, limbal stem cell transplant and amniotic membrane transplant prior to penetrating keratoplasty should be performed. Patients with severe ocular surface disease due to chemical eye injury, Stevens-Johnson syndrome may undergo deep lamellar keratoplasty. Deep lamellar keratoplasty has a lower risk of allograft rejection. Children with

multiple graft failures, severe ocular surface disease may need Boston Keratoprosthesis (KPro).

Perioperative Care

Success of corneal transplant surgery is determined by meticulous peri-operative care. Thorough examination of child including slit lamp biomicroscopy should be performed. During the follow-up visits parents should be explained danger signs and should be asked to report immediately if any such signs appear. Infants and younger children do not communicate their symptoms. However, if the child is irritable or crying without any obvious cause, then should be brought for eye check-up. The first examination is usually at 24 hours interval. Infants or children should be examined daily for one week and then alternate days for next two weeks followed by once weekly examination. We examine the status of the graft clarity, wound integrity, epithelial healing, intraocular inflammation and intraocular pressure every visit. Parents should be counseled to take precautions and avoid any kind of trauma/injury. We have treated several children for post trauma wound dehiscence.

Complications:

Early

The common problems encountered in the first few days are disruption of host graft junction, fibrinous reaction and high intraocular pressure. Infective keratitis although rare (5%) may occur and needs intensive topical antibacterial treatment. Fibrinous exudative reaction should be treated with topical and systemic steroids. Delay in epithelization may be secondary to severe uveitis or high intraocular pressure. In these cases severe uveitis is treated with topical or systemic steroids. Once uveitis or high intraocular pressure is controlled, epithelial defect heals completely. Rarely endophthalmitis following penetrating keratoplasty in children may occur.

Intermediate

Neonates and infants need to be examined under general anaesthesia at around 3 weeks even if they have no visible problem. Wound healing in neonates and infants is fast and sutures become loose. At 3 to 4 weeks loose suture should be removed. At 6-8 week complete healing occurs and sutures may be removed. Older children (2 to 4 years) may be observed for loose suture and may be removed little later. Children above 6 years behave more or less similarly to adults and selective suture removal may be performed.

Late Complications

Allograft rejection, suture related infections, recurrence of disease (HSK, keratoconus), post keratoplasty astigmatism and post keratoplasty glaucoma may occur. Suture related complications can be prevented by immediate removal of loose sutures which may cause an epithelial defect, secondary inflammation and trigger allograft rejection due to inflammation and graft vascularization. Post keratoplasty astigmatism is higher with PKP as compared to lamellar procedure (LK/DALK). Selective suture removal can be done to reduce astigmatism in children aged 6 years of more. Although rare, post-PK traumatic wound dehiscence may occur and requires emergency treatment.

Allograft Rejection

Parents should be explained that allograft rejection might occur any time after surgery. Neonates and infants should be closely monitored for development of allograft rejection in the first year of life as graft failure occurs most frequently during this period (Lee et al, 2016; Hutcheson 2007). Pediatric patients have tendency for more postoperative inflammation, increasing the risk of synechiae formation and rejection (O'Hara & Mannis 2013; Vanathi et al, 2009; Reidy 2001). Children are unable to complain about the symptoms and usually present late for treatment. Parents should be

educated to bring the child for examination on observing any signs like redness, discomfort, opacity in the graft or decrease in vision. On every visit slit-lamp examination should be done to detect early signs of allograft rejection though infants and children may not present with the characteristic signs. Graft edema even in the absence of keratic precipitates should also be treated as allograft rejection. Intra ocular pressure should be monitored in these cases, as they may have associated secondary glaucoma. Once allograft rejection is diagnosed, the child is put on prednisolone acetate (0.1%) eye drop every one hour and atropine ointment twice daily. In addition oral prednisolone (1 mg/kbw) should also be prescribed. In recent studies topical cyclosporine A (2%) has been found successful in treating graft reaction (Cosar et al, 2003). It has also been used to prevent

graft rejection in high risk cases. Cyclosporine A being lipid soluble, topical cyclosporine A (2%) needs to be prepared in castor oil in the hospital pharmacy. At times young children may not tolerate it, as it causes significant ocular irritation. It has also been reported to cause persistent epithelial defects and delayed epithelial healing. Recent studies have shown that topical cyclosporine A prepared in the aqueous solution is also effective and can be prepared in preservative free artificial tear solution. Topical cyclosporine A 0.05% (Restasis, Allergan) has been found effective in treatment and prevention of graft rejection in high risk cases and reported to be equally effective in concentrations ranging from 0.05% to 1%. The formulation of the drug is such that it releases large number of micro-droplets in the tear film.



Figure 1

- (a) Bilateral congenital corneal opacity. (b) Bilateral acquired corneal opacities.
 (c) Unilateral acquired corneal opacity. (d) Healed corneal laceration for RG P contact lens fitting.

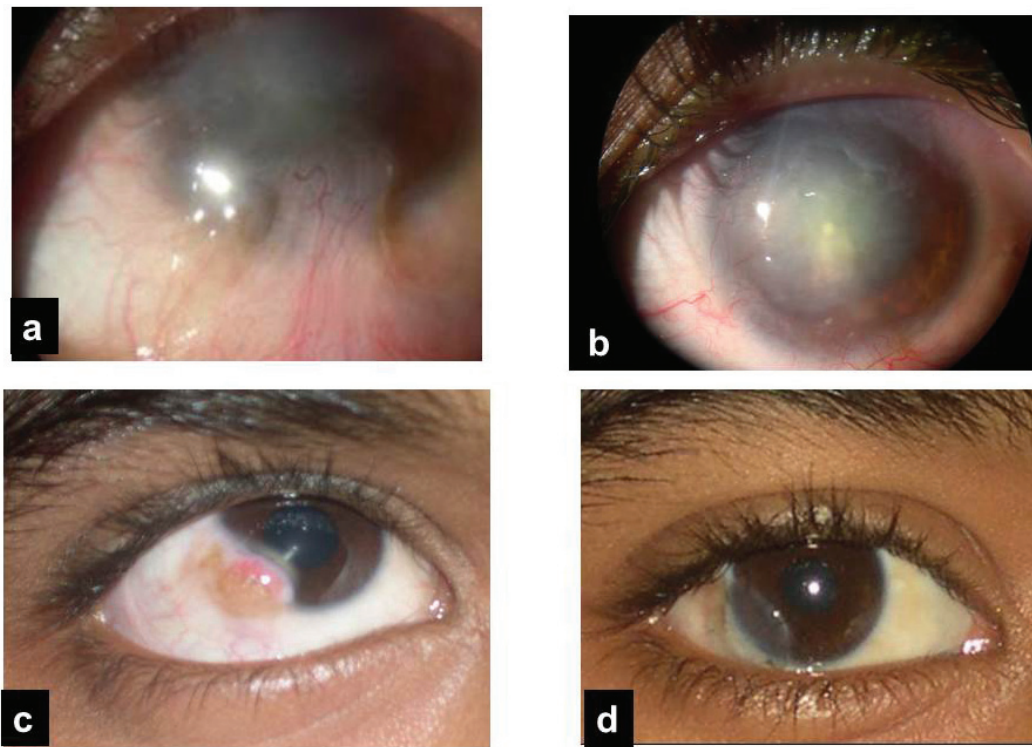


Figure 2: Chemical Eye Injury
(a) Before amniotic membrane transplant. (b) After amniotic membrane transplant
(c) Limbal dermoid (c) pre-operative (d) post surgery, DALK.

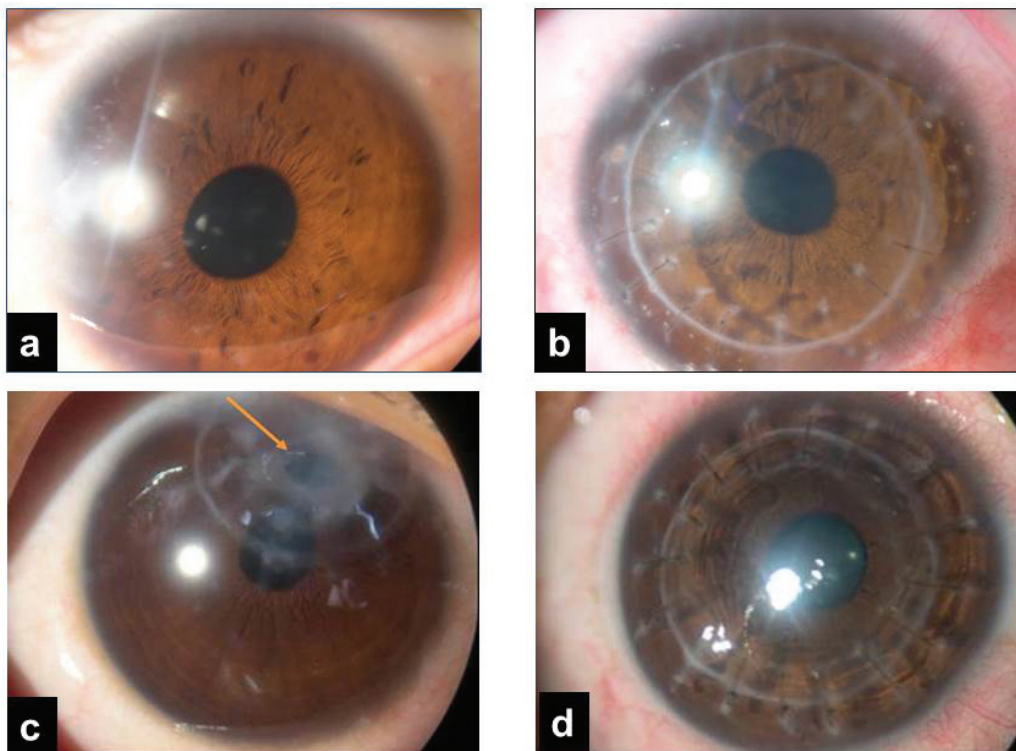


Figure 3: (a) DALK for multiple stromal foreign bodies (Pre op)
(b) DALK for multiple stromal foreign bodies (Post op)
(c) DALK for chronic corneal perforation with anterior staphyloma (Arrow corneal perforation) (d) Penetrating keratoplasty for keratoconus.

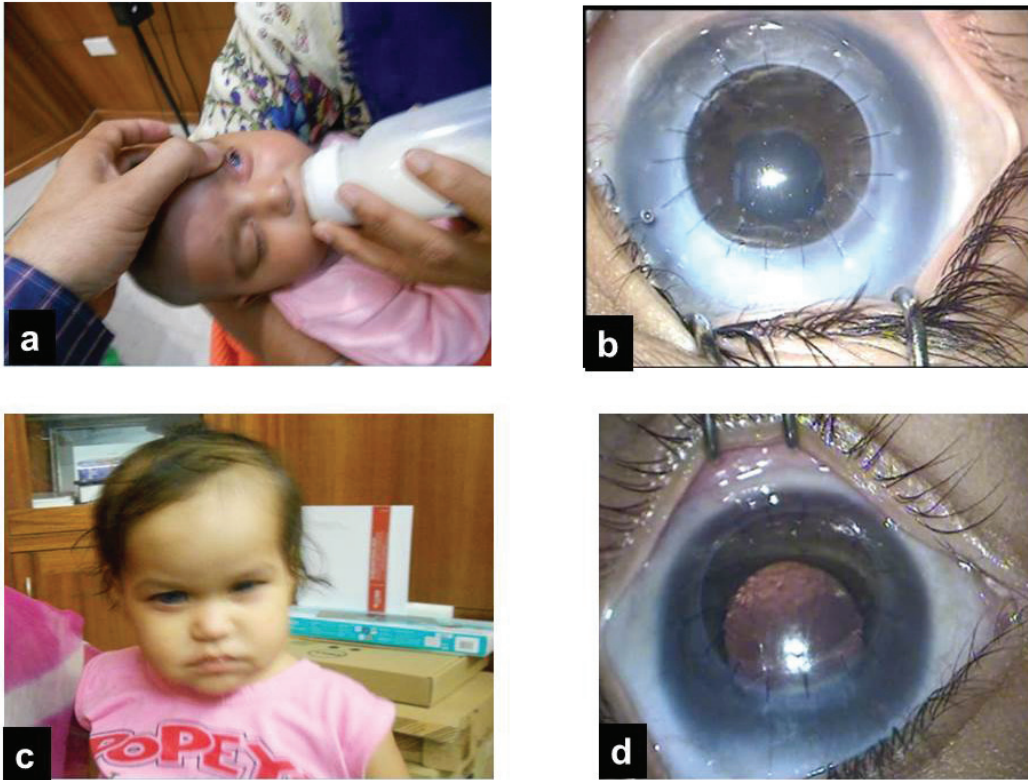


Figure 4: Penetrating keratoplasty in children with buphthalmos and opaque cornea
 (a) Neonate (2 months) post PKP day 1
 (b) Clear graft after 3 years of PKP
 (c) Child with bilateral PKP
 (d) R/E of same patient clear graft after 7 years PKP

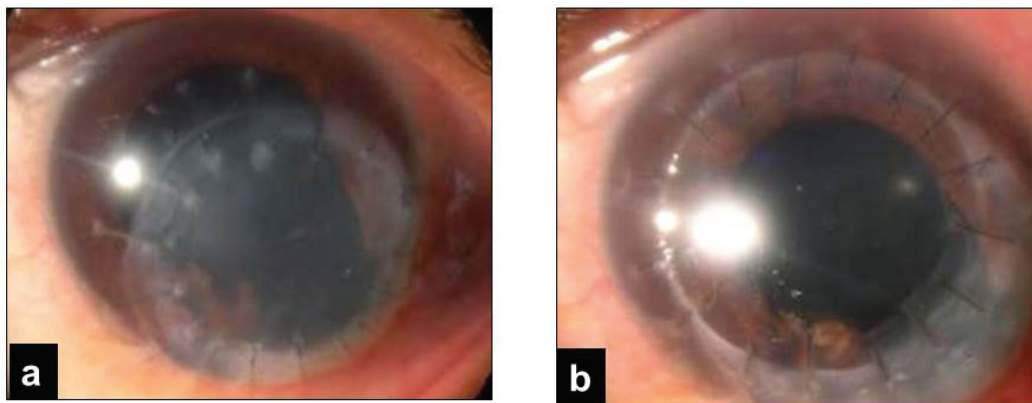


Figure 5: Regraft for opaque therapeutic graft
 (a) Before regrant
 (b) After regrant

Glaucoma

Treatment of glaucoma prior to or post-PK includes medical treatment, trabeculectomy

with adjuvants and/or trabeculotomy. Treatment of refractory glaucoma is a real challenge as it will not only damage the optic nerve but also

corneal endothelium resulting in graft failure. Glaucoma drainage implant procedures have shown encouraging results in the treatment of post-PK refractory glaucoma (Al-Torbak 2004). Several authors have reported favorable results of pediatric penetrating keratoplasty following control of IOP using glaucoma drainage implant procedures. Although conventionally, first glaucoma is controlled and only then is penetrating keratoplasty performed. At times due to the risk of irreversible amblyopia development, glaucoma implant surgery may be combined with PK to enable early visual rehabilitation.

Treatment of Amblyopia

Following surgery amblyopia treatment should be started as early as possible. Cycloplegic refraction should be done and glasses should be prescribed. Parents should be explained that the patching of normal eye so that the patient uses the operated eye. The schedule for patching may be the same as used for standard amblyopia treatment. In children upto 2 years (2:1), 2 to 3 years (3:1), 3 to 4 years (4:1), 4 to 5 years (5:1) and 6 years or above (6:1) should be used.

Outcome

Studies show a better graft survival rate in cases of acquired opacities versus congenital ones (upto 85% versus 50-90%) (Dana et al, 1995; Patel et al, 2005; Al-Ghamdi et al, 2007; Stulting et al, 1984). Anatomical success rate following penetrating keratoplasty in childhood including infants and neonates has increased significantly. The incidence of vision restoration in children following penetrating keratoplasty is still low. Visual prognosis has been reported to be better in younger children and is likely determined by the incidence and severity of amblyopia. In recent study of 65 grafts on 58 eyes of 52 children (mean age 10.6 years SD 4.3 years) 38% achieved BCVA 6/9 or better and 60% had BCVA 6/18 or better (Patel et al, 2005). Visual

acuity has been reported to be significantly better for the acquired indications as compared to the congenital corneal conditions. Significant number of patients in this study had keratoconus as an indication for PKP (Fig 3d). Results from developing countries are less favorable. In a study from India, nearly 1/3rd patients achieved $> \text{ or } = 20/400$ vision and nearly 50% of these achieved $> \text{ or } = 20/50$ (Aasuri et al, 2000). Allograft rejection, infective keratitis and glaucoma were major causes of graft failure. The overall long term (10 years) probability of maintaining clear graft after initial penetrating keratoplasty for Peter's anomaly is 35% \pm 0.6% (Yang et al, 1999). Eyes with severe disease, larger donor cornea, co-existing central nervous system abnormalities and anterior synechiae were reported to have significantly poorer outcome than the eyes without these factors. Children with severe form of Peter's anomaly may require multiple grafts to have functional vision. Children with congenital glaucoma and corneal scarring after glaucoma filtering surgery are benefitted by performing PKP. We have performed PKP on 21 such children and 16 had clear graft on last follow up (Fig. 4a,b,c,d)

Repeat Corneal Graft

In case the child develops graft failure a repeat graft should be considered. Parents need to be explained that subsequent corneal grafts have less chances of success. In a study (Dana et al, 1995) 20% of eyes underwent re-grafts at a mean of 17 months after first graft. The graft success rate decreased from 78% in primary grafts to 19% in two grafts but nil success in eyes with three grafts. In another series, 6 of the 16 eyes in 10 patients underwent regrafts (2 or more) over a mean follow up period of 30 months (Parmley et al, 1993). Repeat graft may be indicated to prevent dense and irreversible amblyopia. However in case the child is having unilateral corneal opacity, parents should be explained that even if the graft may becomes

opaque, chances of improvement of vision later on by performing repeat graft can be expected. In adults it is advisable to wait for 6 months in cases of graft rejection, before a repeat graft is performed. It is aimed to bring down the inflammation in the graft to minimum and to decrease the incidence of allograft rejection. At times it may be difficult to ascertain whether the graft failed due to allograft rejection or due to some other cause. It is better to treat it as allograft rejection. In younger children it may not be possible to wait for 6 months due to danger of development of amblyopia. In these cases the repeat graft may be performed at 3 months after the initial graft has failed. One can wait a little longer in case the child is six year old or more. Children suffering from perforated corneal ulcers need therapeutic penetrating keratoplasty and these grafts usually become opaque due to chronic inflammation. However, successful regraft can be performed in these patients at a later date and both vision improvement and graft clarity can be obtained (Fig 5a,b).

Keratoprosthesis

Infants and children who are at high risk of graft rejection and subsequent graft failure may be benefited with keratoprosthesis or artificial corneal transplantation (Botelho et al, 2006). Keratoprosthesis transplantation means placing an optical device in the host cornea. It is immunologically inert and has the advantage that graft rejection does not occur. Recently, a custom made Boston type 1 keratoprosthesis is available and can be designed to correct refractive errors including aphakia. AlphaCor, a synthetic cornea made up of hydrophilic polymer poly (2-hydroxyethyl methacrylate) is another keratoprosthesis used in high risk cases for corneal transplant surgery (Ilhan-Sarac & Akpek 2005). The AlphaCor is implanted in a corneal stromal lamellar pocket in a two stage procedure. In the first stage 360° peritomy and debridement of corneal epithelium is done. A

superior 180° limbal incision at 50% of depth is extended into the corneal stroma forming an intralamellar pocket. A central 3.5 mm posterior corneal trephination is performed. The device is placed within the corneal pocket and paralimbal incision is closed. After 8 to 12 weeks anterior trephination (3mm) is done to expose the optic of the device. Keratoprosthesis helps the corneal surgeon to rehabilitate those corneal blinds having visual potential, but who are unlikely to be benefited by performing penetrating keratoplasty using human donor cornea.

Pediatric corneal transplant surgery is a team effort it involves combined effort of corneal surgeon assisted by glaucoma specialist, pediatrician, anaesthetist, counsellors and rehabilitation team.

Rehabilitation of blinds due to corneal disease

Children with bilateral corneal opacities either congenital or post chemical burns, Stevens Johnson Syndrome may not be successfully visually rehabilitated even after performing repeated corneal grafts. The parents of these children should be counselled to get their children admitted to blind schools to provide educational and vocational training to these children. These children can lead independent life and contribute to the development of the society if proper facilities and opportunities are provided.

Summary & Conclusions

Advancement in micro-surgical techniques, quality eye banking and better anaesthesia facilities have made it possible to undertake corneal transplant in a neonate as soon as the diagnosis is made and corneal transplant surgery advised. Although surgery is technically demanding but it is possible to provide clear visual axis during critical period of visual development. Penetrating keratoplasty remains the gold standard however DALK and DSAEK

may be considered when indicated. Treatment and prevention of development of amblyopia in neonates is extremely important even after successful penetrating keratoplasty.

References

- Aasuri MK, Garg P, Gokhle N, Gupta S (2000). Penetrating keratoplasty in children. *Cornea*; 19:140-4.
- Al-Ghamdi A, Al-Rajhi A, Wagoner MD (2007). Primary pediatric keratoplasty: Indications, graft survival, and visual outcome. *J Am Assoc Pediatr Ophthalmol Strabismus*; 11:1:41-47.
- Al-Torbak AA (2004). Outcome of combined Ahmed glaucoma valve implant and penetrating keratoplasty in refractory congenital glaucoma with corneal opacity. *Cornea*; 23:554-9.
- Anwar HM, El-Danasoury A (2014). Endothelial keratoplasty in children. *Curr Opin Ophthalmol*; 25:4:340-346.
- Botelho PJ, Congdon NG, Handa JT, Akpek EK (2006). Keratoprosthesis in high-risk pediatric corneal transplantation: first 2 cases. *Arch Ophthalmol. Sep*; 124:1356-7.
- Bourne WM, Brubaker RF (1978). A method for ipsilateral rotational autokeratoplasty. *Ophthalmology*; 85:1312-1316.
- Cosar CB, Laibson PR, Cohen EJ, Rapuano CJ (2003). Topical cyclosporine in pediatric keratoplasty. *Eye Contact Lens*; 29:103-7.
- Dada T, Sharma N, Vajpayee RB (1999). Indications for pediatric keratoplasty in India. *Cornea*; 18:296-8.
- Dana MR, Moyes AL, Gomes JA et al (1995). The indications for and outcome in pediatric keratoplasty. A multicenter study. *Ophthalmology*; 102:1129-38.
- de Laage de Meux P (2000). Modern therapeutic approach to congenital abnormalities of the anterior eye segment in pediatric patients. *J Fr Ophthalmol*; 23:908-16. French.
- Hashemi H, Ghaffari R, Mohebi M (2012). Posterior lamellar keratoplasty (DSAEK) in Peters anomaly. *Cornea*; 31:10:1201-1205.
- Hestle RW, Oslin SE (1997). Successful visual rehabilitation after neonatal penetrating keratoplasty. *B J Ophthalmology*; 81:644-48.
- Hutcheson K (2007). Application of new ophthalmic technology in the pediatric patient. *Curr Opin Ophthalmol*; 18:5:384-391.
- Ilhan-Sarac O, Akpek EK (2005). Current concepts and techniques in keratoprosthesis. *Curr Opin Ophthalmol*; 16:246-50.
- Kasmann-Kellner B, Weindler J, Pfau B, Ruprecht KW (1999). Ocular changes in mucopolysaccharidosis IV A (Morquio A syndrome) and long-term results of perforating keratoplasty. *Ophthalmologica*. 1999;213:200-5.
- Koenig SB (1986). Myopic shift in refraction after penetrating keratoplasty with pediatric donor tissue. *Am J Ophthalmol*; 101:740-1.
- Kymionis GD, Kankariya VP, Diakonis VF, Karavitaki AE, Siganos CS, Pallikaris IG (2012). Descemet stripping automated endothelial keratoplasty in a child after failed penetrating keratoplasty. *J AAPOS*; 16:1:95-6.
- Lee, Olivia, Lenhart, Phoebe and Stulting D (2016). Pediatric Penetrating Keratoplasty. *Cornea. Bd Chapter 12.* ;1455.
- Miller D, Atebara N, Stegam R (1989). The optical quality of peripheral cornea. *Acta Ophthalmol*; 67:165-170.
- Nirankari VS, Sharma A. Personal Communication.



O'Hara M, Mannis MJ (2013). Pediatric penetrating keratoplasty. *Int Ophthalmol Clin*; 53:2:59–70.

Palay DA, Kangas TA, Stulting RD, Winchester K, Litoff D, Krachmer JH (1997). The effects of donor age on the outcome of penetrating keratoplasty in adults. *Ophthalmology*; 104:1576-9.

Panda A, Bhageshwar LM, Ray M, Singh J P, Kumar A (1999). Deep lamellar keratoplasty versus penetrating keratoplasty for corneal lesions. *Cornea*; 18:172-5.

Parmley VC, Stonecipher KG, Rowsey JJ (1993). Peter's anomaly: a review of 26 penetrating keratoplasties in infants. *Ophthalmic Surg*; 24:31—5

Parrish CM, Faris DA, O'Day DM (1988). Mattress bridge sutures for graft fixation in pediatric keratoplasty: new use of an old technique. *Ophthalmic Surg*; 19:795-8.

Patel HY, Ormonde S, Brookes NH, Moffatt LS, McGhee CNJ (2005). The indications and outcome of paediatric corneal transplantation in New Zealand: 1991-2003. *Br J Ophthalmol*; 89:4:404–408.

Reidy JJ (2001). Penetrating keratoplasty in infancy and early childhood. *Curr Opin Ophthalmol*; 12:4:258–261.

Shousha MA, Yoo SH, Kymionis GD (2011). Long-term results of femtosecond laser-assisted sutureless anterior lamellar keratoplasty. *Ophthalmology*; 118:2:315–323.

Smiddy WE et al (1989). Contact lenses for visual rehabilitation after corneal laceration repair. *Ophthalmology*; 96:293:298.

Stulting RD, Summers KD, Cavanagh HD, Waring GO, Gammon JA (1984). Penetrating Keratoplasty in Children. *Ophthalmology*; 91:10:1222–1230.

Toker E, Seitz B, Langenbacher A, Dietrich T, Naumann GO (2003). Penetrating keratoplasty for endothelial decompensation in eyes with buphthalmos. *Cornea*; 22:198-204.

Vajpayee RB, Ramu M, Panda A, Sharma N, Tabin GC, Anand JR (1999). Oversized grafts in children. *Ophthalmology*; 106:829-32.

Vanathi M, Panda A, Vengayil S, Chaudhuri Z, Dada T (2009). Pediatric Keratoplasty. *Surv Ophthalmol*; 54:2:245–271.

Walls P, Micheli-Cohan A, Abdolell M, Rootman D (2000). Outcome of lamellar keratoplasty for limbal dermoid in children. *JAAPOS*; 6:209-15.

Yang LL, Lambert SR, Lynn MJ, Stulting RD (1999). Long term results of graft survival in infant and children in Peter's anomaly. *Ophthalmology*; 106:833-48.

Yoo S, Goldman D, Karp CL, Brien TPO, Culbertson WW, Alfonso EC (2008). Femtosecond laser-assisted sutureless anterior lamellar keratoplasty. *Ophthalmology*; 115:8:1303–1308.