Review Article

A review of techniques and outcomes of endothelial keratoplasty in congenital hereditary endothelial dystrophy

Sohini Mandal, Mohamed I Asif, Prafulla K Maharana, Namrata Sharma, Jeewan S Titiyal

Congenital hereditary endothelial dystrophy affects the Descemet membrane and endothelium, resulting in corneal decompensation. Penetrating keratoplasty (PKP) has been the gold-standard surgical management until recently; however, at present, endothelial keratoplasty (DSEK/DSAEK/n-DSEK: Descemet-stripping or non-Descemet stripping endothelial keratoplasty and DMEK/n-DMEK: Descemet membrane endothelial keratoplasty) is being preferred due to lesser intraoperative and postoperative complications, early visual recovery, and comparable visual outcomes. Endothelial keratoplasty (EK) can be challenging, especially in pediatric eyes with CHED due to smaller eyeballs, shallow anterior chambers, phakic status, and poor intraoperative visibility due to thick and hazy corneas. A total of 198 articles matched our search strategy. After screening for duplication and going through the titles and abstracts, 12 relevant original articles, one case series, and six case reports were included in this review. Various surgical modifications have to be adopted in comparison to adult eyes to overcome the aforementioned difficulties. Regardless, studies have shown favorable visual outcomes with better graft survival and fewer complications in eyes that underwent EK compared to PKP. Hence, timely surgical intervention and strict amblyopia management can result in better final visual outcomes. The purpose of this review is to summarize various intraoperative difficulties and the surgical modifications required, different surgical techniques, visual and graft-related outcomes, and various complications of EK in CHED eyes.

Key words: Congenital hereditary endothelial dystrophy, Descemet membrane endothelial keratoplasty, Descemet stripping automated endothelial keratoplasty, endothelial keratoplasty

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Congenital hereditary endothelial dystrophy (CHED), an autosomal recessive disorder, is characterized by bilateral corneal clouding with a ground-glass appearance and focal gray spots due to stromal edema and Descemet membrane (DM) thickening.[1] Symptoms include decreased vision and nystagmus, with minimal tearing and photophobia often resulting in amblyopia. Although the primary pathology lies in the DM and endothelium, until recently, penetrating keratoplasty (PKP) has been the gold-standard surgical treatment.[2-7]

Corneal transplantation in children is challenging even for experienced surgeons, resulting in increased complications due to various factors such as small eyeballs, low scleral rigidity, shallow anterior chamber, phakic status, and increased positive vitreous pressure.[8] Children are often difficult to examine and are more prone to trauma, infection, and allograft rejection. These factors contribute to the high incidence of graft failure following PKP.[6,9,10] Today, endothelial keratoplasties such as Descemet stripping endothelial keratoplasty (DSEK), Descemet-stripping automated endothelial keratoplasty (DSAEK), and Descemet membrane endothelial keratoplasty (DMEK) are preferred over PKP due to a decrease in the rates of suture-related complications, complications of open-sky procedures, graft rejection/failure, unstable refractive outcomes, and the need for multiple examinations under anesthesia. The effectiveness of DMEK in the management of CHED has been very recently documented in the literature with favorable visual outcomes.[11-14]

Performing EK in CHED patients is associated with various intraoperative difficulties: poor visibility due to severe corneal edema and strong adherence of the DM to the underlying stroma, which may result in DM retention/tags, leading to graft detachment and failure.[15,16] DM scoring is found to be much simpler in decompensated corneas such as Fuchs' endothelial dystrophy in contrast to the CHED eyes.[17]

In this review, we attempt to cover various surgical techniques, visual and refractive outcomes, graft-related outcomes, and complications related to endothelial keratoplasty (EK) in CHED patients.

Methods

A literature search was performed using PubMed (United States National Library of Medicine), Embase (Reed Elsevier

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Properties SA), Web of Science (Thomson Reuters), and Scopus (Elsevier BV) by using the following keywords: congenital hereditary endothelial dystrophy and Descemet stripping endothelial keratoplasty or Descemet stripping automated endothelial keratoplasty or Descemet membrane endothelial keratoplasty or endothelial keratoplasty or pediatric DMEK. A total of 198 articles matched our search strategy. After screening for duplication and going through the titles and abstracts, 12 relevant original articles, one case series, and six case reports were included in this review.

All relevant articles, including case reports, were also included in this review. All other studies of pediatric EK due to other causes of congenital corneal opacity have been excluded from this review. Reference lists from the selected articles were further screened to obtain further relevant articles.

Results

We herein describe the outcomes of DSAEK and DMEK in cases of CHED.

DSAEK in CHED

DSAEK graft offers clear advantages over PKP for the treatment of endothelial failure in the pediatric age group as it is performed under a "closed system," minimizing the risk of intraoperative complications.[18] Since the first published series of DSAEK in CHED by Busin *et al*., several publications have shown that DSAEK is a safe and effective surgery in providing rapid restoration of corneal clarity with fewer complications compared to PKP.[19-30]

1. *Surgical Technique*

Different techniques have been defined by various authors in their studies. To reduce the posterior vitreous pressure, intravenous mannitol 20% is routinely given for all CHED cases before beginning the procedure. The approach to the surgery might be superior or temporal cornea as per the surgeon's preference.[18-30]

a. Donor tissue preparation: The donor lenticules can be either prepared preoperatively by trained technicians and appropriately stored (pre-cut donor lenticules) or they can be cut at the time of the surgery either by manual dissection or by using an automated lamellar therapeutic keratoplasty (ALTK) system.[22,26,28,29] Manual dissection can be done using Melles blunt dissectors and a Moria or Barron artificial anterior chamber.[17,20,21,23,25,30] A graduated diamond knife can help decide the depth of dissection depending on the donor thickness.[17] The automated system uses microkeratome blades of various head sizes (blade depth: 300–400 μm).[18,20,24,27] Femtosecond laser can also be used, which allows the precise creation of dissection planes.[22,23] Following lamellar dissection, the posterior donor lamella is cut using disposable hand-held punches depending on the white-to-white diameter of the recipient.[18,22,25,29,30] The lenticules remained well attached during the postoperative period irrespective of the donor tissue preparation method. The reported incidence of graft detachment following DSEK is 0%–82%, and that after DSAEK is 0%–43%.[31-34] The highly variable rate is due to the heterogeneity in the inclusion parameters in various studies.

b. Recipient bed preparation: Gentle debridement of host epithelium usually aids in better visualization in edematous corneas.[17,22,25,27,29] A circular marker (7.5–9.0 mm) using gentian violet can be used to outline the limits of the internal surface from which DM-endothelium has to be peeled off.[18-21,24,29] The area of DM removal is usually 1 mm larger in diameter than the planned donor graft. Phakic DSAEK is considered challenging in terms of both intraoperative difficulties and the risk of subsequent cataract formation. Mechanical damage during the procedure may be a contributing factor in the development of early or latent secondary cataracts. Safety measures such as using viscoelastic devices, pupil constriction so the iris acts as a barrier, and maintaining the anterior chamber using a constant inflow of air or saline should be adopted to prevent lenticular trauma. The incision sites can be moved approximately 1 mm superiorly from the standard 9- and 3-o'clock positions so that the entire graft pull-through maneuver is performed using the superior part of the iris to protect the underlying crystalline lens.[18,19] [Fig. 1] Despite these strategies, the incidence of post-DSAEK cataracts has been reported between 7% and 37%.[31,35] Trypan blue (0.06%) solution can also be used to increase the visibility of DM through the edematous cornea.[24,25,30] [Fig. 1] Chandelier illumination has been proven to improve visualization during DM stripping and graft centration.[17,21]

DM scoring is more difficult to perform in eyes with CHED. Most surgeons demonstrated successful descemetorrhexis with reverse Sinskey hook [Fig. 1]; however, Busin *et al*.[18] and Lenhart *et al*.[26] used cystotome to carefully cut through the DM in cases with adherent DM. Scoring can also be performed using a cannula, Terry scraper, or DM stripper and forceps.[18,20,26,27] Descemetorrhexis can be performed under balanced salt solution, air, or viscoelastic material depending on the surgeon's preference.[17-30] Poor visibility due to severe corneal edema and strict adherence of DM to underlying stroma, especially in infants, makes descemetorrhexis difficult to accomplish in CHED eyes.[18,19,21,23,28,29] However, there are no significant differences in visual or graft-related outcomes with any of these techniques.[22]

However, stripping the DM has several disadvantages, especially in recipients with severe corneal edema. The scope of the stripped DM is difficult to control, which may result in incomplete donor graft coverage and persistent edema postoperatively. In contrast, n-DSAEK, which does not require the removal of the DM, has its own merits. It has been shown to simplify the procedure, shorten the surgical time, and reduce inflammatory reactions. n-DSAEK is preferred in cases where DM cannot be identified, such as in infants (age less than 1 year),[18,19,21] poor visibility due to severe corneal edema,[28,29] and when DM stripping is difficult even after numerous attempts.[27]

c. Donor lenticule insertion: Lenticule insertion and unfolding are technically challenging, and a rise in IOP should be avoided to reduce the chance of lenticule dropout. Donor lenticule can be introduced into the anterior chamber by using different techniques such as combined use of Busin glide and suture-assisted donor lenticule insertion; alternatively, the donor lenticule can be loaded onto Busin glide, Sheet's IOL glide, or Tan Endoglide and pulled into the AC by using an internal limiting membrane peeling forceps from the clear corneal side port on the opposite end.[17-30] The donor graft can be placed as a 60/40 under fold or 50/50 "taco" configuration and inserted into the

AC.[22,29] However, Price *et al*.[36] reported that curling the DSAEK graft into a cylindrical shape for insertion causes less endothelial cell loss and improved graft longevity than folding the graft for insertion. To prevent postoperative pupillary block, a peripheral iridectomy should be performed and a complete air fill in the AC should be maintained for 10 min. Partial-thickness venting incisions till the graft interface at a 45° angle is a good option in cases where the graft is found to be excessively mobile due to interface fluid.[17] This is followed by the partial release of air to maintain 60%–75% air volume in the AC [Fig. 1]. Variable time periods for postoperative maintenance of supine position have been recommended, ranging from 2 h, 4h, and up to 12 h.[18-20,22,24,29]

Table 1 summarizes the preoperative parameters and surgical techniques of DSAEK in CHED.

2. *Outcomes of DSAEK in CHED*

a. Visual outcomes
In various studies, the preoperative corrected distance visual acuity (CDVA) ranged from counting fingers to 20/63.[18,20,22] Improvement in vision in pre-verbal children and infants was as early as 1 week to up to 2 years of follow-up.[18,19,22,28] Similar results were found in older children, whose postoperative CDVA ranged from 20/160 at 12 months follow-up to near 20/20 (0.03 logMAR) at 2–9 years follow-up.[18,19,21,22,26] This wide range can be attributed to different preoperative visual acuity, varied age at surgery, amblyopia, and surgeon's bias.

b. Refractive outcomes
EK is associated with a lower and more predictable postoperative refractive error with early stabilization. This offers an added advantage for better amblyopia management, less frequent change of glasses, and better compliance of the parents to therapy**.** DSAEK grafts usually induce a hyperopic of 0.75–1.5 D.[38,39] Postoperative cycloplegic refraction in CHED eyes ranged from − 7 DS to + 10 DS (up to 4 DC) in various studies.[17-19,21,23,25-27,30] In one of the largest case series by Mohebbi *et al*.,[22] the residual postoperative refractive error was + 2.57 ± 3.3 DS in the age group of 3–16 years at follow-up of 38 months.

c. Graft-related outcomes
Though the cornea becomes relatively clear following successful EK, the clarity never reaches the pristine quality of PKP due to the stromal–stromal interface haze. Despite this, the visual acuity remains comparable between groups.[23] It may be claimed that persistent haze may by itself account for amblyopia and decrease in contrast; however, early visual stabilization, predictable refraction, and avoiding suture-related complications might offer more advantages in terms of amblyopia management.[23] All corneas are expected to clear between 1 week and a month following EK, and clarity continues to improve until a year.[17-21,23,25] Infants seem to have a faster improvement in corneal clarity compared to older children due to the lesser duration of pre-existed corneal edema.[20] Due to the stromal–stromal interface in DSEK, residual haze is often present until a year.[25-27,29,30] Graft detachment or dislocation is the most common graft-related complication postoperatively and can be managed with re-bubbling on the immediate postoperative day.[18-21,23,26,28,30] Slight graft decentration may be observed without any need for intervention.[26,28] Other less common complications include immunologic graft rejection, which can be easily reverted with topical and systemic steroids, and graft failure due to traumatic wound dehiscence.[19,22]

d. Complications
There were no intraoperative complications, such as lenticular touch, in any of the case series. However, the completion of DM scoring was not attempted in a few cases either due to incomplete visualization or very adherent DM, especially in infants.[18,19,21,23,28,29] DM tags were left in place in a few cases even after unsuccessful attempts of DM removal.[26,27] Mohebbi *et al*.[22] reported a case of pupillary block on the first postoperative day and increased IOP in 61.1% of cases. Yang *et al*.[20] demonstrated that infants show a lower rate of complications, faster recovery, and better outcomes of DSAEK compared to children >1 year of age as infants are more likely to remain supine postoperatively for graft attachment and commencement of amblyopia management at an earlier age.

Table 2 summarizes the visual, refractive, and graft-related outcomes and complications of DSAEK in CHED.

DMEK in CHED

DMEK, a recent addition to EK, is advantageous over DSAEK due to relatively faster visual recovery and a lower rejection rate. DMEK has been ineffectively attempted in an infant's eye with posterior polymorphous corneal dystrophy, whereas it has shown good visual and functional outcomes in a Kearns–Sayre syndromic child with endothelial dysfunction.[40,41] To date, only four studies have evaluated the anatomical and functional outcomes of DMEK and n-DMEK in CHED eyes.[11-14]

1. *Surgical Technique*

a. Donor tissue preparation: In all the studies, donor DM stripping was performed intraoperatively before DMEK surgery by using a standard approach.[11-14] After scoring of the peripheral endothelium–Descemet membrane (EDM), it is carefully separated from the underlying stroma by using a pair of McPherson forceps under 1–2 drops of the storage medium (submerged cornea under backgrounds away technique) till 1–2 mm short of completion such that a peripheral hinge of stromal–EDM adhesion is left. The stripped EDM is floated back using the storage medium, leaving one-half of the corneal stroma exposed for the creation of a stromal window. The inked F-stamp/S-mark is lightly applied to DM through the 2-mm stromal window with the replacement of the stromal plug.[42]

b. Recipient bed preparation: DM stripping is performed encompassing a larger area of 9 mm in CHED eyes with thickened DM that can be visualized preoperatively on ASOCT. Saad *et al*. and Fogla *et al*. reported 57% and 50% of CHED eyes to have thickened DM, respectively; however, Fogla *et al*. recommended DM stripping in all cases irrespective of the DM morphology.[11-13]

c. Donor lenticule insertion: A glass injector connected to a fluid-filled syringe is used to insert the donor lenticule into the AC. After securing the main wound with 10-0 nylon sutures, a no-touch tapping technique is used to unroll the lenticule.[11,13] The graft unfolding and correct orientation can be confirmed by the F-stamp/S-mark and Mi-OCT. For tamponade to support the donor DM, air or 20% sulfur hexafluoride gas can be injected, especially in

Table 1: Summary of the preoperative parameters and surgical techniques of endothelial keratoplasty in CHED

Authors	Age group	No. of eyes undergoing DSAEK/DMEK	No. of eyes undergoing n-DSAEK/n-DMEK	Type of approach	Type of lenticule dissection	Technique of lenticule insertion	Additional modifications	Type of tamponading agent	Postoperative positioning with timing
Busin *et al.*[18]	6 months -30 yrs	9	6	Superior	Microkeratome	Busin glide	Incisions sites shifted 1 mm superiorly from The standard 3 and 9 o'clock position	Air	Supine for 2 h
Madi *et al.*[19]	6 months -16 yrs	7	6	Superior	ALTK Moria system	Dye-less, Baron punch, Busin glide	Incisions sites shifted 1 mm superiorly from standard 3 and 9 o'clock position Venting incisions till the interface	Air	Supine for 2 h
Yang *et al.*[20]	6 months-13 yrs	30	0	Superior	Microkeratome in 26 eyes Manual in 4 eyes (flexible tissue)	Combination of suture pull-through and Busin glide	--	Air	Supine for 4 h
Ashar *et al.*[17]	5-12 yrs	5	0	Superior	Manual (Barron's artificial chamber, Melles dissectors, graduated diamond knife)	Sheet's IOL glide	Chandelier illumination assisted DM Stripping Venting incisions in 2 cases (excessively mobile lenticule)	Air	--
Ashar *et al.*[21]	4-7 yrs	3	3	Superior	2 eyes: Moria microkeratome 3 eyes: Manual by Barron's artificial anterior chamber 1 eye: Femtosecond laser	Sheet's IOL glide	Chandelier illumination ensured graft centration	Air	Supine for several hours
Mohebbi *et al.*[22]	3-16 yrs	18	0	Temporal	Microkeratome	13 eyes: 60/40 underfold 4 eyes: Busin glide 1 eye: Tan Endoglide	--	Air	Supine for 12 h
Ashar *et al.*[23]	4-10 yrs	2	3	Superior	2 eyes: Barron's artificial anterior chamber 2 eyes: Moria ALTK system 1 eye: Femtosecond	Sheet's IOL glide	Chandelier illumination assisted DM stripping Push in or pull through technique	Air	--
Vajpayee *et al.*[24]	-	3	0	Superior	Moria microkeratome	Busin glide assisted	--	Air	Supine for 2 h

Contd...

Table 1: Contd...

Authors	Age group	No. of eyes undergoing DSAEK/DMEK	No. of eyes undergoing n-DSAEK/n-DMEK	Type of approach	Type of lenticule dissection	Technique of lenticule insertion	Additional modifications	Type of tamponading agent	Postoperative positioning with timing
Goshe *et al.*[37]	8 yrs	2	0	--	Pre-cut tissue	Charlie's insertion forceps by folding it 40/60	Scraping of the recipient bed	Air	Supine till next day
Lenhart *et al.*[26]	8 months	1	0	Superior	Pre-cut tissue	Sheet's IOL glide	Difficult DM stripping (adherent) Venting incision	Air	--
Anwar *et al.*[27]	10 yrs	0	1	Superior	Moria microkeratome	Busin glide	Failed attempt of DM stripping	Air	Supine for 3-4 days
Bellucci *et al.*[28]	3 months	0	2	Temporal	Manual, Pre-cut	Busin glide	--	Air	--
Panahi-Bazaz *et al.*[29]	19 yrs	0	1	Temporal	Pre-cut	Suture pull through (50-50),	--	Air	Supine for 2 h
Mittal *et al.*[25]	19 yrs	1	0	--	--	Busin glide	--	Air	--
Mittal *et al.*[30]	2.5-3.5 yrs	3	0	--	--	Sheet's IOL glide	--	Air	--
Saad *et al.*[11]	2-23 yrs	8	6	Temporal	Manual stripping	Glass injector connected to a fluid-filled syringe	DM stripping done in cases with thickened DM only	Air (DMEK) or SF6 20% (nDMEK)	Supine for 24 h
Fogla *et al.*[12]	3-39 yrs	6	6	Temporal	Manual stripping	Glass injector connected to a fluid-filled syringe	DM stripping done in cases with thickened DM only	Air	Supine for 24 h
Fogla *et al.*[13]	10-23 yrs	15	0	Temporal	Manual stripping	Glass injector connected to a fluid-filled syringe	--	Air	Supine for 24 h
Srinivasan *et al.*[14]	6-15 yrs	5	2	Temporal	Manual stripping	Glass injector connected to a fluid-filled syringe	DM stripping done of the same size as the graft	Air	Supine for 24 h

Table 2: Summary of visual, refractive, and graft-related outcomes and complications of endothelial keratoplasty in CHED

Authors	Age group	Follow-up time (months)	No. of eyes	Pre-op visual acuity	Post-op complications	Post-op visual acuity	Post-op Refraction	Graft condition at last follow-up
Busin *et al*.[18]	6 months-30 yrs	15.9	15	No FF-20/70	4 graft detachment	FF–≥20/40	−0.5 to+7.75 DS	Clear-centered graft
Madi *et al*.[19]	6 months-16 yrs	14.5	13	No FF-20/70	4 graft dislocation 1 rejection	FF–≥20/40	−4DS to+10 DS (0.5–3 DC)	Clear-centered graft
Yang *et al*.[20]	6 months-13 yrs	48±22.8	30	No FF-logMAR 1.03±0.25	3 graft detachment	logMAR 0.32–0.54±0.20	--	Clear-centered graft
Ashar *et al*.[17]	5-12 yrs	12	5	FC@1/2m- 20/125	Nil	20/160–20/50	−7 to+8 DS (up to−2 DC)	Clear-centered graft
Ashar *et al*.[21]	4-7 yrs	12	6	1.13–1.3 logMAR	1 graft detachment in nDSAEK case	0.13±0.10 logMAR	−2 to+6 DS (up to+2 DC)	Clear-centered graft
Mohebbi *et al*.[22]	3-16 yrs	38	18	No FF-20/63	1 pupillary block on POD1 Raised IOP (61.1%) 1 graft failure at 9 months 1 graft failure at 30 months	FF–20/40	+2.57±3.3 DS	15 clear-centered grafts 1 faintly hazy graft 2 failed grafts
Ashar *et al*.[23]	4-10 yrs	12	5	<0.05	2 graft dislocation	0.37±0.17 logMAR	3.5±4.18 DS (−1.6±2.6 DC)	All clear grafts: PK>DSAEK Clear-centered graft
Vajpayee *et al*.[24]	-	6	3	1.3–3 logMAR	Nil	0.3–0.48 logMAR	--	Residual corneal haze
Goshe *et al*.[37]	8 yrs	13	2	20/100	Nil	20/50	−1.25 to+0.50 DS (+0.75–2.5 DC)	Clear-centered graft
Lenhart *et al*.[26]	8 months	24	1	central, steady, maintained	Nil	--	+0.75 DS±0.8 DC	Clear-centered graft
Anwar *et al*.[27]	10 yrs	12	1	FC@1m	Nil	20/100	+4 DS (−0.5 DC)	Moderate residual stromal haze
Bellucci *et al*.[28]	3 months	10	2	No FF	Slight temporal decentration in 1 eye	FF	--	Clear-centered graft
Panahi-Bazaz *et al*.[29]	19 yrs	4	1	HMCF	Nil	FC@4m	--	Residual corneal haze
Mittal *et al*.[25]	19 yrs	6	1	FCCF	Nil	20/100	+2 DC	Slight corneal haze
Mittal *et al*.[30]	2.5-3.5 yrs	16–20	3	Identify objects close to the face	Partially dislocated graft and interface fluid in 1 eye	20/60	+3 to+5 DS (−1.5 to−2 DC)	Subtle stromal haze in 1 eye, Clear-centered graft in 2 eyes
Saad *et al*.[11]	2-23 yrs	16.9±8.1	14	0.9±0.3	2 aqueous misdirection 3 Donor DM detachment in DMEK 1 Donor DM detachment in nDMEK 1 graft failure	0.4±0.2	--	Clear-centered graft
Fogla *et al*.[12]	3-39 yrs	17.6±6.8	12 6- nDMEK 6-DMEK	1.15 (nDMEK) 0.95 (DMEK)	1 (nDMEK)- donor DM detachment	0.37 (nDMEK) 0.25 (DMEK)	--	Clear-centered graft

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Table 2: Contd...

Authors	Age group	Follow-up time (months)	No. of eyes	Pre-op visual acuity	Post-op complications	Post-op visual acuity	Post-op Refraction	Graft condition at last follow-up
Fogla *et al.*[13]	10-23 yrs	7.8±2.5	15	0.8±0.3	Nil	0.3±0.2	--	Clear-centered graft with unusual folds in the anterior stroma
Srinivasan *et al.*[14]	6-15 yrs	--	5	1.93±0.25	1 primary graft failure 2 graft detachment; required rebubbling	0.98±0.29	--	Well-attached scroll with a more transparent cornea (80%)

FF- fix and follow; FC- finger counting; FCCF- finger counting close to face; HMCF- hand movement close to face; IOP- intraocular pressure; logMAR- logarithm of the minimum angle of resolution; POD- postoperative day.

non-stripping Descemet membrane EK (nDMEK) cases for longer tamponade.[12]

Table 1 summarizes the preoperative parameters and surgical techniques of DMEK in CHED.

2. *Outcomes of DMEK in CHED*

a. Visual outcomes

Saad *et al*.[11] showed a significant improvement in CDVA from 0.9 ± 0.3 to 0.4 ± 0.2 logMAR irrespective of stripping or non-stripping of DM at 16.9 ± 8.1 months. Similarly, Fogla *et al*.[12] reported marked improvement in the mean CDVA from 0.8 ± 0.3 to 0.3 ± 0.2 logMAR at 7.8 ± 2.5 months. A study comparing standard DMEK versus nDMEK demonstrated only a minor visual gain in either group and similar outcomes between both groups. This could be due to amblyopia as most of these patients were operated on at an older age (13–39 years).

b. Refractive outcomes

DMEK is associated with minimal changes in the refractive error, that is, surgically induced corneal astigmatism of <1 D and a minimal change in the spherical equivalent of 0.5–1 D induced at the anterior corneal surface.[43] This is because the DM graft has an equal thickness over its entire diameter unlike that of DSAEK.[44,45]

c. Graft related outcomes

Following DMEK, the stromal collagen fibers seem to appear more compact on ASOCT, with a reduction in corneal thickness. Corneal thickness was shown to decrease significantly in all studies from 991 ± 65 μm to 590 ± 70 μm following DMEK and 895 ± 51 μm to 603 ± 46 μm following nDMEK.[11-13] Average endothelial cell loss (ECL) at 6 months after routine DMEK ranges from 25% to 47%.[46] The mean ECL in CHED eyes following DMEK was 33% at 16.9 ± 8.1 months (32.3% in the nDMEK group and 33.6% in the DMEK group at 17.6 ± 6.8 months and 10.5 ± 4 months, respectively).[11,12] These data suggest that ECL following DMEK is comparable to DSAEK in CHED eyes. Fogla *et al*.[13] reported the presence of abnormal corneal folds in the anterior stroma in one-third of the eyes despite having a good resolution of corneal edema. These folds were restricted to the anterior stroma of the recipient cornea, suggesting that this could be due to the rapid resolution of corneal edema and an accompanying change in corneal curvature. This could be because the collagen fibers in the posterior half of the cornea become more compact following DMEK than the anterior half because of the poor water retentive capacity of keratan sulfate, resulting in a possible curvature mismatch between them. In addition, the anterior collagen fibers have greater rigidity, making them less pliable after the resolution of edema.[47] A similar appearance has been noted postoperatively following DSAEK in CHED.[17,20]

d. Complications

i. Intraoperative: Due to repeated intraocular manipulation during difficult DM stripping, a case of intraoperative aqueous misdirection has been reported that was managed with pars plana core vitrectomy.[11]

ii. Postoperative: Donor graft detachment is the most common postoperative complication, which could be related to eye rubbing or failure to maintain a supine position, with a reported incidence of 0%–43%.[33,34] Graft failure was noted in a single case at the 5-month follow-up and required a repeat DMEK surgery.[11]

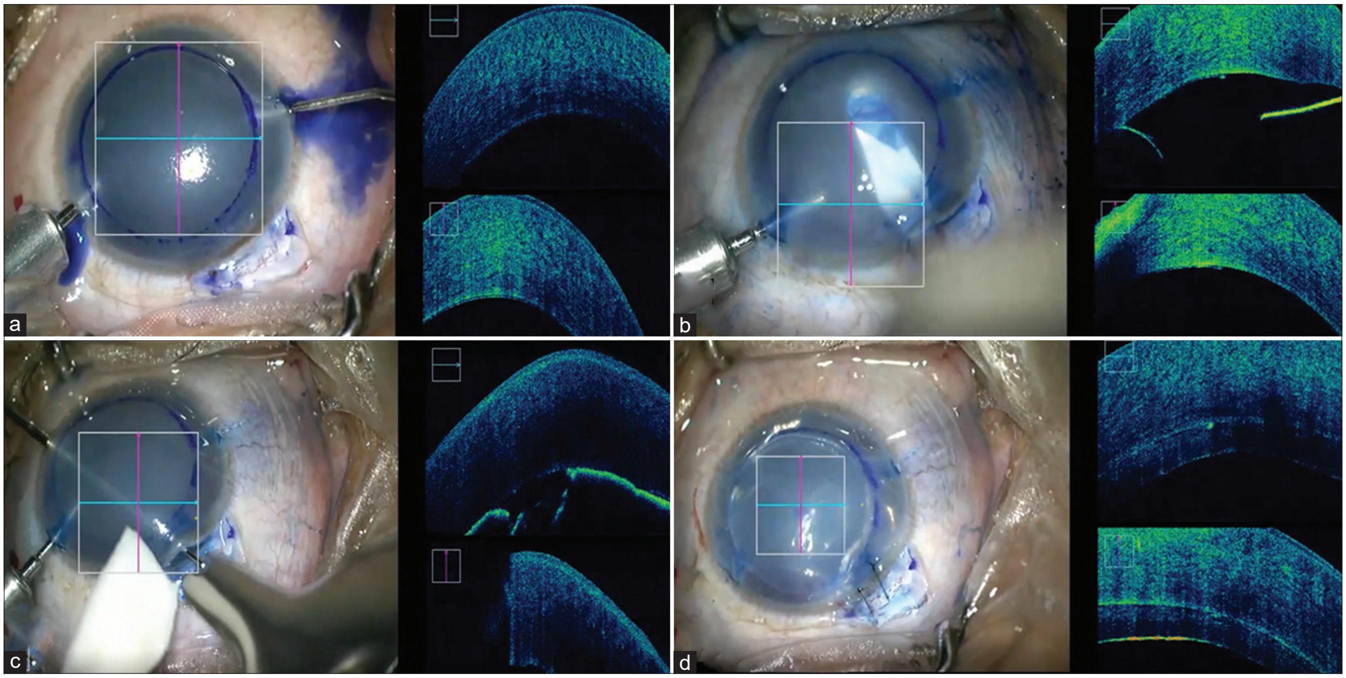

Figure 1: Descemet stripping endothelial keratoplasty in CHED eye: (a) Injection of Trypan blue dye 0.06% into the anterior chamber for better visualization of Descemet membrane during scoring by using a reverse Terry–Sinskey hook; (b) A metallic instrument such as the crescent blade is inserted beneath the detached DM after descemetorhexis to highlight the stained DM for better visualization; (c) Wounds for insertion of donor tissue are shifted superiorly from their regular 9- and 3-o'clock positions such that during graft delivery, forceps does not pass across the pupil and the iris protects the underlying crystalline lens from any possible contact with the instrument; (d) Air injection to maintain 75% air volume in the anterior chamber and visualization of double ring sign, suggesting the correct graft orientation

Table 2 summarizes the visual, refractive, and graft-related outcomes and complications of DMEK in CHED.

Discussion

EK can be challenging, especially in children. Good visual outcomes can be achieved following EK in CHED eyes if intervened early with effective amblyopia management. Although the optimal age for EK remains controversial, early surgical intervention should be advocated to avoid amblyopia. EK should be preferred over PKP due to lesser complications, early visual recovery and refractive stability, better amblyopia management, and comparable visual outcomes. AlArrayedh *et al*.[48] demonstrated poor outcomes from PKP in CHED due to dense amblyopia and a high risk of long-term graft failure.

Various intraoperative difficulties discussed require adequate surgical expertise to efficiently address them. The DM remnants/tags that might hinder the graft apposition and lead to detachment can be visualized better and removed using intraoperative chandelier illumination, intraoperative OCT, or by using the metal surface of the crescent blade against the stained DM.[49-52] Ashar *et al*.[17] compared DSEK with and without Descemet stripping and concluded similar outcomes. Similar results were reported by Asif *et al*.[51] that there was no significant difference in terms of graft detachment irrespective of whether DM was stripped in CHED eyes.

Partial and peripheral graft detachment following DMEK rates have been reported for around 62%–63% and complete detachment for around 30%; however, with improved techniques and surgical experience, this has significantly reduced to 34.6% in a multicenter study and to as low as 4% in one case series.[53-55] Therefore, a learning curve for DMEK surgery, including postoperative care, is highly relevant.[56-58]

Intraoperatively, graft adhesion can be confirmed by the double ring sign; however, this is not always possible in CHED eyes due to thick and hazy corneas.[59] An acute-angled bevel sign on Mi-OCT can also be useful in confirmation of the graft orientation in these cases.[60] During DMEK, the staining of the donor DM and the S-mark/F-stamp can facilitate in visualizing and confirming the orientation of the graft intraoperatively. The orientation of the DM scroll in the AC can also be confirmed using Mi-OCT intraoperatively before air tamponade.

Conclusion

To conclude, EK is a preferred treatment in CHED eyes, and it can be performed safely with certain modifications compared to that in adults. EK can be planned early to prevent the development of amblyopia. EK results in optimal visual and refractive outcomes compared to PKP with much lesser complications.

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Conflicts of interest

There are no conflicts of interest.

References

1. Weiss JS, Møller HU, Aldave AJ, Seitz B, Bredrup C, Kivelä T, *et al*. IC3D classification of corneal dystrophies--edition 2. Cornea 2015;34:117-59.
2. Schaumberg DA, Moyes AL, Gomes JAP, Dana MR. Corneal transplantation in young children with congenital hereditary

endothelial dystrophy: Multicenter pediatric keratoplasty study. Am J Ophthalmol 1999;127:373-8.

3. Kirkness CM, McCartney A, Rice NSC, Garner A, Steele AD. Congenital hereditary corneal oedema of Maumenee: Its clinical features, management, and pathology. Br J Ophthalmol 1987;71:130-44.
4. Sajjadi H, Javadi MA, Hemmati R, Mirdeghan A, Parvin M, Nassiri N. Results of penetrating keratoplasty in CHED: Congenital hereditary endothelial dystrophy. Cornea 1995;14:18-25.
5. Al-Rajhi AA, Wagoner MD. Penetrating keratoplasty in congenital hereditary endothelial dystrophy. Ophthalmology 1997;104:956-61.
6. Al-Ghamdi A, Al-Rajhi A, Wagoner MD. Primary pediatric keratoplasty: Indications, graft survival and visual outcome. J AAPOS 2007;11:41-7.
7. Pearce WG, Tripathi RC, Morgan G. Congenital endothelial corneal dystrophy: Clinical, pathological, and genetic study. Br J Ophthalmol 1969;53:577-91.
8. Vanathi M, Panda A, Vengayil S, Chaudhuri Z, Dada T. Pediatric keratoplasty. Surv Ophthalmol 2009;54:245-71.
9. Wagoner MD, Al-Ghamdi AH, Al-Rajhi AA. Bacterial keratitis after primary pediatric penetrating keratoplasty. Am J Ophthalmol 2007;143:1045-7.
10. Huang PT. Penetrating keratoplasty in infants and children. J AAPOS 2007;11:5-6.
11. Saad A, Ghazzal W, Keaik M, Indumathy TR, Fogla R. Outcomes of Descemet's membrane endothelial keratoplasty for congenital hereditary endothelial dystrophy. J AAPOS 2020;24:358.e1-6. doi: 10.1016/j.jaapos. 2020.07.018.
12. Fogla R. Role of anterior segment OCT for Descemet membrane stripping during Descemet membrane endothelial keratoplasty in eyes with congenital hereditary endothelial dystrophy. Cornea 2021;40:458-61.
13. Fogla R, Srinivasan B. Corneal folds after Descemet membrane endothelial keratoplasty in congenital hereditary endotheial dystrophy. Cornea 2021;40:715-19.
14. Srinivasan B, Agarwal M, Iyer G, Agarwal S, Padmanabhan P. Pediatric Descemet membrane endothelial keratoplasty. Am J Ophthalmol 2021;227:12-7.
15. Pineda R, Jain V, Shome D, Hunter DC, Natarajan S. Descemet's stripping endothelial keratoplasty: Is it an option for congenital hereditary endothelial dystrophy? Int Ophthalmol 2010;30:307-10.
16. Nikolic L, Jovanovic V, Lackovic V, Todorovic V. Endothelial keratoplasty without Descemet's membrane stripping: Histologic and ultrastructural findings. Ophthalmic Res 2010;43:56-60.
17. Ashar JN, Madhavi Latha K, Vaddavalli PK. Descemet's stripping endothelial keratoplasty (DSEK) for children with congenital hereditary endothelial dystrophy: Surgical challenges and 1-year outcomes. Graefes Arch Clin Exp Ophthalmol Albrecht Von Graefes Arch Klin Exp Ophthalmol 2012;250:1341-5.
18. Busin M, Beltz J, Scorcia V. Descemet-stripping automated endothelial keratoplasty for congenital hereditary endothelial dystrophy. Arch Ophthalmol 2011;129:1140-6.
19. Madi S, Santorum P, Busin M. Descemet stripping automated endothelial keratoplasty in pediatric age group. Saudi J Ophthalmol. 2012;26 (3):309-13.
20. Yang F, Hong J, Xiao G, Feng Y, Peng R, Wang M, *et al*. Descemet stripping endothelial keratoplasty in pediatric patients with congenital hereditary endothelial dystrophy. Am J Ophthalmol 2020;209:132-40.
21. Ashar JN, Ramappa M, Chaurasia S. Endothelial keratoplasty without Descemet's stripping in congenital hereditary endothelial dystrophy. J AAPOS 2013;17:22-4.
22. Mohebbi M, Nabavi A, Fadakar K, Hashemi H. Outcomes of Descemet-stripping automated endothelial keratoplasty in congenital hereditary endothelial dystrophy. Eye Contact Lens 2020;46:57-62.
23. Ashar JN, Ramappa M, Vaddavalli PK. Paired-eye comparison of Descemet's stripping endothelial keratoplasty and penetrating keratoplasty in children with congenital hereditary endothelial dystrophy. Br J Ophthalmol 2013;97:1247-9.
24. Vajpayee RB, Maharana PK, Jain S, Sharma N, Jhanji V. Thin lenticule Descemet's stripping automated endothelial keratoplasty: Single, slow pass technique. Clin Exp Ophthalmol 2014;42:411-6.
25. Mittal V, Mittal R, Sangwan VS. Successful Descemet stripping endothelial keratoplasty in congenital hereditary endothelial dystrophy. Cornea 2011;30:354-6.
26. Lenhart PD, Evans CT, Beck AD, Lee WB. Visual outcome after Descemet's stripping automated endothelial keratoplasty in an 8-month-old with congenital hereditary endothelial dystrophy. J AAPOS 2013;17:637-9.
27. Anwar HM, El Danasoury A, Hashem A. Descemet's stripping automated endothelial keratoplasty for congenital hereditary endothelial dystrophy. Clin Ophthalmol 2012;6:159-63.
28. Bellucci R, Chierego C, Bellucci C. Endothelial keratoplasty in a newborn baby with CHED. Cornea 2011;30:1488-90.
29. Panahi-Bazaz M, Sharifipour F, Malekahmadi M. Modified Descemet's stripping automated endothelial keratoplasty for congenital hereditary endothelial dystrophy. J Ophthalmic Vis Res 2014;9:522-5.
30. Mittal V, Mittal R. Challenges in pediatric endothelial keratoplasty. Indian J Ophthalmol. 2014;62:251-4.
31. Price FW, Price MO. Descemet's stripping with endothelial keratoplasty in 200 eyes: Early challenges and techniques to enhance donor adherence. J Cataract Refract Surg 2006;32:411-8.
32. Mearza AA, Qureshi MA, Rostron CK. Experience and 12-month results of Descemet-stripping endothelial keratoplasty (DSEK) with a small-incision technique. Cornea 2007;26:279-83.
33. Lee WB, Jacobs DS, Musch DC, Kaufman SC, Reinhart WJ, Shtein RM. Descemet's stripping endothelial keratoplasty: Safety and outcomes: A report by the American Academy of Ophthalmology. Ophthalmology 2009;116:1818-30.
34. Covert DJ, Koenig SB. Descemet stripping and automated endothelial keratoplasty (DSAEK) in eyes with failed penetrating keratoplasty. Cornea 2007;26:692-6.
35. Tsui JY, Goins KM, Sutphin JE, Wagoner MD. Phakic Descemet stripping automated endothelial keratoplasty: Prevalence and prognostic impact of postoperative cataracts. Cornea 2011;30:291-5.
36. Price MO, Bidros M, Gorovoy M, Price FW Jr, Benetz BA, Menegay HJ, *et al*. Effect of incision width on graft survival and endothelial cell loss after Descemet stripping automated endothelial keratoplasty. Cornea 2010;29:523-7.
37. Goshe JM, Li JY, Terry MA. Successful Descemet's stripping automated endothelial keratoplasty for congenital hereditary endothelial dystrophy in a pediatric patient. Int Ophthalmol 2012;32:61-6.
38. Koenig SB, Covert DJ, Dupps WJ Jr, Meisler DM. Visual acuity, refractive error, and endothelial cell density six months after Descemet stripping and automated endothelial keratoplasty (DSAEK). Cornea 2007;26:670-4.
39. Jun B, Kuo AN, Afshari NA, Carlson AN, Kim T. Refractive change after Descemet stripping automated endothelial keratoplasty surgery and its correlation with graft thickness and diameter. Cornea 2009;28:19-23.
40. Hermina Strungaru M, Ali A, Rootman D, Mireskandari K. Endothelial keratoplasty for posterior polymorphous corneal dystrophy in a 4-month-old infant. Am J Ophthalmol Case Rep 2017;7:23-6.

41. Gonnermann J, Klamann MK, Maier AK, Bertelmann E, Schroeter J, von Au K, *et al*. Descemet membrane endothelial keratoplasty in a child with corneal endothelial dysfunction in Kearns-Sayre syndrome. Cornea 2014;33:1232-4.
42. Veldman PB, Dye PK, Holiman JD, Mayko ZM, Sáles CS, Straiko MD, *et al*. Stamping an S on DMEK donor tissue to prevent up-side-down grafts: Laboratory validation and detailed preparation technique description. Cornea 2015;34:1175-8.
43. Price MO, Giebel AW, Fairchild KM, Price FW Jr. Descemet's membrane endothelial keratoplasty; prospective multicenter study of visual and refractive outcomes and endothelial survival. Ophthalmology 2009;116:2361-8.
44. Holweger RR, Marefat B. Corneal changes after cataract surgery with 5.0 mm sutures and 3.5 mm sutureless clear corneal incisions. J Cataract Refract Surg 1997;23:342-6.
45. Olsen T, Dam-Johansen M, Bek T, Hjortdal JO. Corneal versus scleral tunnel incision in cataract surgery: A randomized study. J Cataract Refract Surg 1997;23:337-41.
46. Deng SX, Lee WB, Hammersmith KM, Kuo AN, Li JY, Shen JF, *et al*. Descemet membrane endothelial keratoplasty: Safety and outcomes: A report by the American Academy of Ophthalmology. Ophthalmology 2018;125:295-310.
47. Bron AJ. The architecture of the corneal stroma. Br J Ophthalmol 2001;85:379-81.
48. AlArrayedh H, Collum L, Murphy CC. Outcomes of penetrating keratoplasty in congenital hereditary endothelial dystrophy. Br J Ophthalmol 2018;102:19-25.
49. Shimizu T, Hayashi T, Yuda K, Tsuchiya A, Oyakawa I, Mizuki N, *et al*. Chandelier illumination for Descemet membrane endothelial keratoplasty. Cornea 2017;36:1155-7.
50. Inoue T, Oshima Y, Hori Y, Maeda N, Nishida K. Chandelier illumination for use during Descemet stripping automated endothelial keratoplasty in patients with advanced bullous keratopathy. Cornea 2011;30(Suppl 1):S50-3.
51. Asif MI, Bafna RK, Sharma N, Kaginalkar A, Sinha R, Agarwal T, *et al*. Microscope integrated optical coherence tomography guided Descemet stripping automated endothelial keratoplasty in congenital hereditary endothelial dystrophy. Clin Ophthalmol 2021;15:3173-81.
52. Sharma N, Sharma VK, Arora T, Singh KR, Agarwal T, Vajpayee RB. Novel technique for Descemet membrane remnant stripping in hazy cornea during DSAEK. Cornea 2016;35:140-2.
53. Guerra FP, Anshu A, Price MO, Giebel AW, Price FW. Descemet's membrane endothelial keratoplasty: Prospective study of 1-year visual outcomes, graft survival, and endothelial cell loss. Ophthalmology 2011;118:2368-73.
54. Guerra FP, Anshu A, Price MO, Price FW. Endothelial keratoplasty: Fellow eyes comparison of Descemet stripping automated endothelial keratoplasty and Descemet membrane endothelial keratoplasty. Cornea 2011;30:1382-6.
55. Ang M, Wilkins MR, Mehta JS, Tan D. Descemet membrane endothelial keratoplasty. Br J Ophthalmol 2016;100:15-21.
56. Price FW Jr, Price MO. Endothelial keratoplasty to restore clarity to a failed penetrating graft. Cornea 2006;25:895-9.
57. Caldwell MC, Afshari NA, Decroos FC, Proia AD. The histology of graft adhesion in Descemet stripping with endothelial keratoplasty. Am J Ophthalmol 2009;148:277-81.
58. Kobayashi A, Yokogawa H, Sugiyama K. Non-Descemet stripping automated endothelial keratoplasty for endothelial dysfunction secondary to argon laser iridotomy. Am J Ophthalmol 2008;146:543-9.
59. Delfazayebaher S, Feizi S, Javadi MA, Baradaran-Rafii A, Sadoughi MM, Faramarzi A. Double-ring sign to confirm correct orientation of donor lenticules during Descemet stripping automated endothelial keratoplasty. Cornea 2015;34:980-4.
60. Titiyal JS, Kaur M, Shaikh F, Bari A. "Acute-angled bevel" sign to assess donor lenticule orientation in ultra-thin Descemet stripping automated endothelial keratoplasty. BMJ Case Rep 2019;12:e227927.