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REVIEW

Changing Strategies in Keratoplasty After Corneal Hydrops: From Penetrating to Lamellar Approaches – A Narrative Review

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Abstract: The hallmark of acute corneal hydrops (CH) is Descemet membrane (DM) rupture that leads to the influx of fluid into the cornea causing corneal edema. Multiple risk factors have been related to an increased incidence of CH in keratoconus (KC) patients, such as Down's syndrome, atopy, vernal keratoconjunctivitis, eye rubbing, and an earlier age of KC onset. Penetrating keratoplasty (PKP), deep anterior lamellar keratoplasty (DALK), compression sutures, cyanoacrylate tissue adhesive with bandage contact lens (BCL), intracameral gas injection, and amniotic membrane transplant (AMT) are some of the conservative and surgical methods used to treat CH. Compared to KC without a history of CH, the need for PKP in patients with healed hydrops is higher due to preexisting DM rupture. Thus, the majority of surgeons conduct PKP after CH. On the other hand, some corneal surgeons choose to perform DALK over PKP as it spares the host endothelium. In this narrative review, we compare DALK to PKP for corneal hydrops in KC, evaluating the challenges, advantages, and visual and refractive outcomes.

Keywords: keratoconus, visual rehabilitation, corneal transplantation, lamellar keratoplasty, graft survival, corneal hydrops

Introduction

Keratoconus (KC) is a non-inflammatory degenerative corneal ectasia that exhibits progressive steepening and protrusion of the cornea, which results in a loss of visual acuity.[1] The prevalence of the disease in the general population varies considerably among different regions of the world. A recent meta-analysis found that keratoconus affected 1.38 per 1000 population [95% confidence interval (CI): 1.14–1.62 per 1000].[2] The etiology and pathogenesis of the disease are still not fully understood however, associations have been reported with chronic eye rubbing, rigid gas-permeable contact lens wear, atopy, systemic conditions such as Down syndrome, Leber's congenital amaurosis, and connective tissue disorders.[3] There are multiple staging or classification systems for ectatic disease. The Amsler-Krumeich (AK) classification was the oldest and most widely used system until the more comprehensive Belin ABCD classification or staging system was published.[4]

Acute corneal hydrops (CH) is a clinical condition characterized by Descemet membrane (DM) rupture, resulting in fluid influx into the cornea and eventually corneal edema.[5] Many risk factors have been linked to an increased risk of CH in KC patients, including Down's syndrome, atopy, vernal keratoconjunctivitis, eye rubbing, and an earlier age of KC onset. The most significant risk factor appears to be eye rubbing.[6]

An ancillary test that helps diagnose acute CH is anterior segment optical coherence tomography (AS-OCT), which shows an intrastromal hyporeflective area of fluid and disruption of the DM.[7] Treatment of CH aims to alleviate symptoms and shorten recovery, which includes both conservative and surgical options such as intracameral gas

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injection, cyanoacrylate tissue adhesive with bandage contact lens (BCL), compression sutures, and amniotic membrane transplantation (AMT), penetrating keratoplasty (PKP), and deep anterior lamellar keratoplasty (DALK).[5]

This narrative review aims to compare the challenges, advantages, and outcomes in KC patients with corneal hydrops who have undergone DALK or PKP.

DALK as a Treatment for Acute Hydrops

Corneal transplantation has been an option after the resolution of the edema in CH. However, PKP can be performed in select circumstances as acute therapy for CH; these cases include corneal perforations,[8] unresolved edema,[9] extensive Descemet tear,[10] and considerable neovascularization.[11]

Although many surgeons do not support performing DALK in patients with acute CH, success outcomes have been reported in some case series. Jacob et al published a paper explaining a modified pre-descemetic DALK technique in nine patients with acute hydrops. At the last follow up visit, all patients had clear graft, even with an area of DM defect. The best corrected visual acuity (BCVA) improved from 0.002 ± 0.005 preoperatively to 0.52 ± 0.13.[12] Mohan et al used this technique in their case report of an acute CH as well. The conservative treatment with steroids, hypertonic saline, and anti-glaucoma medications failed to resolve the hydrops. Subsequently, they attempted fluid drainage and injection of non-expansile 14% perfluoropropane (C3F8) in the anterior chamber, which also failed, and the edema recurred.[13] Then, pre-descemetic DALK was performed, and the patient showed improvement with BCVA reaching 6/9 which was maintained during the three-year follow-up period.[13]

Li et al published another technique in a case series of 21 patients with acute hydrops.[14] Their treatment involves the initial creation of an anterior chamber paracentesis followed by thermokeratoplasty and subsequently antiglaucoma medications and topical 0.1% fluorometholone eye drops. One week after resolution of edema and two weeks from the onset of the hydrops, they performed a modified manual DALK.[14] Li et al reported that in 14 of 21 patients, the DM scars disappeared six months after the procedure, and the mean BCVA was 20/30 at one year postoperatively.[14] They recommended that DALK should be performed before the second week after thermokeratoplasty to reduce stromal scars.[14]

PKP in KC After Healed Hydrops

PKP has been the traditional method of corneal transplantation for managing KC for decades.[15] Roughly, 12% to 20% of KC patients may require corneal transplantation at a relatively younger age.[16] The popularity of PKP can be attributed to its excellent visual outcomes that have been reported in long-term studies.[17]

Scar formation following CH increases the likelihood of undergoing PKP compared to KC cases that do not have hydrops. Tuft et al reported a higher likelihood of endothelial rejection following PKP in eyes with previous hydrops.[18] The higher rejection rate was attributed to corneal neovascularization in eyes with severe allergic conditions. In addition, antigen-presenting cells may invade the cornea in response to inflammation associated with corneal edema.[18] Some risk factors for graft rejection include the longer duration of hydrops and ocular allergic reactions.[19] Meyer et al reported a higher risk of endothelial rejection in patients with previous hydrops, presumably due to associated corneal neovascularization, chronic inflammation, concomitant corneal neovascularization, and/or allergic eye disease.[20] Other associated factors with graft rejection include patient age (less than 25 years old), donor trephination size of 8 mm, and poor clinical attendance.[20] However, Basu et al reported that despite a higher endothelial rejection rate, the long-term graft failure was very low.[19] Notably, PKP can be challenging intraoperatively due to positive vitreous pressure in up to 50% of cases, which it can lead to serious complications in absence of adequate management.[21]

DALK in KC After Healed Hydrops

Recent improvements in DALK techniques have made it a preferable alternative to PKP for some corneal surgeons due to the advantage of sparing the host endothelium, which lowers the risk of graft rejection. These techniques allow complete separation of DM from the posterior stroma (See Figures 1 and 2). Anwar's big-bubble technique requires air injection, which separates the stroma from the DM.[22] Melles et al described a technique that involves filling the anterior chamber with air, followed by blade dissection of the pre-descemetic plane. This technique is classified as pre-descemetic DALK due to preservation of a portion of the recipient stroma. Yet, the authors also reported some micro-perforations using this

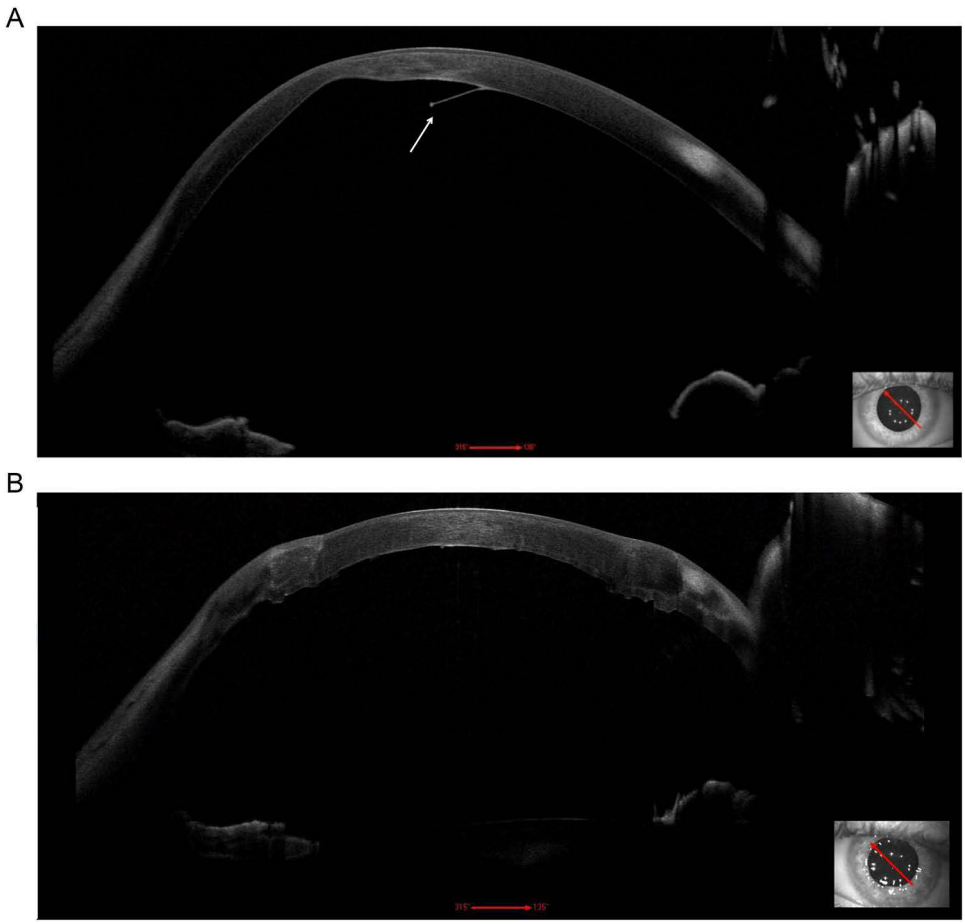

Figure 1 (**A**) Case 1: Image shows preop AS- OCT of a 30-year-old gentleman with advanced KC in left eye (OS) and central thinning with scarring and DM break (depicted by white arrow) as a consequence of previous CH. The red arrow denotes the cross sectional meridional orientation of the scan, running from 315° to 135° across the cornea. (**B**) Case 1: This image shows his 6-month follow up post DALK with minimal central corneal hyperreflectivity and improvement of BCVA from 20/200 to 20/60. The red arrow denotes the cross sectional meridional orientation of the scan, running from 315° to 135° across the cornea.

technique.[23] Navanty and Daya used a modified Melles technique for manual DALK on patients with resolved hydrops.[24] Six out of ten eyes experienced intraoperative micro-perforation at the old hydrops site. They were managed without the need for conversion to PKP.[24] Ramamurthi and Ramesh used a modified technique on four patients using controlled air injection and layer-by-layer dissection of the stroma, but this resulted in perforation at the scar site.[25]

One of the main drawbacks of DALK compared to PKP is the occurrence of intraoperative micro-perforations. These perforations can necessitate a conversion to full thickness PKP.[26] Manual dissection is considered a safer approach due to the lower incidence of perforations compared to the big-bubble technique.[27]

However, in addition to the steep learning curve for this technique, scarring following hydrops makes DALK even more challenging.[28] Despite the success of Anwar's big-bubble technique in patients undergoing DALK, it is not recommended in patients with resolved hydrops because of the attendant risk of intraoperative DM perforation; the new thin layer of DM may not have the tensile strength to adapt to the pressure changes caused by the air bubble injection.[29] However, a recently published retrospective study concluded that DALK with the big bubble technique is a reasonable option for treating hydrops-related corneal scarring, providing similar refractive outcomes to PKP and, surprisingly, less complications.[30] Nevertheless, the surgeon must be prepared to convert to PKP in case of macro-perforations.[30] Furthermore, The size, location, and configuration of DM tears, play an important role in determining the feasibility and safety of DALK after CH, as larger or irregular breaks can alter healing and complicate deep lamellar dissection.[31] AS-OCT shows that the morphology of a DM break evolves over time, emphasizing that the chronology of surgery is important; waiting for scar maturation may improve surgical outcomes and reduce perforation risk.[32]

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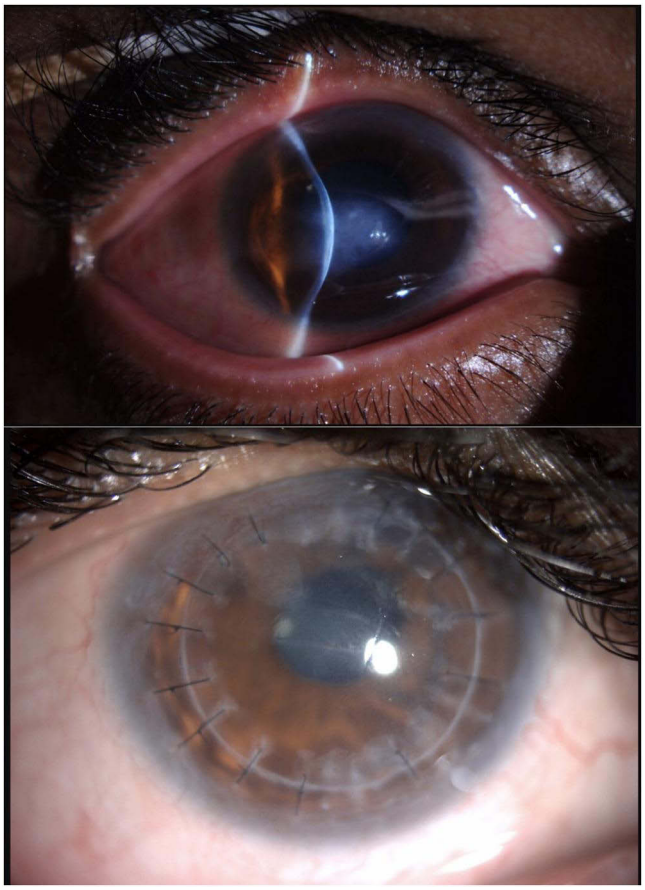

Figure 2 Case 2: Upper image shows preop slit lamp photo of a 27-year-old gentleman with advanced KC and central thinning with scarring and DM detachment as a consequence of previous CH. While the lower image shows his 6-month follow up post DALK with good central corneal clarity and improvement of BCVA from 20/160-1 to 20/60.

Timing After Healed Hydrops

DM tears heal in approximately 4 to 6 months after the incidence of CH.[33] Healing occurs through endothelial migration over the ruptured area.[33] The general recommendation is to wait four months after the occurrence of CH to perform DALK. Scarring can improve corneal contour, allowing the patient to wear a rigid contact lens, delaying the need for early corneal transplantation.[34]

Rejection Risk (Vascularization)

Due to the preservation of healthy endothelium, DALK confers a lower risk of endothelial graft rejection compared to PKP.[35] Although DALK eliminates the risk of endothelial rejection, other types of rejection are still possible.[36] Trimarchi et al found a rejection rate of 4% in PKP patients and 0% in DALK patients.[35] However, the risk for stromal and epithelial rejection following DALK remains.[37] Several studies have reported the occurrence of epithelial and stromal rejection in post-DALK eyes.[35,36] However, effective management can lead to favorable outcomes and a successful recovery in these cases.[35,36]

Endothelial Function

Endothelial cell count and density play an important role in graft survival and the likelihood of requiring subsequent regrafting. This makes DALK superior to PKP since it has minimal effects on the endothelium. Kim et al compared DALK and PKP performed in the eyes of the same patients.[36] They reported lower endothelial cell density in the PKP group. The difference was significant at 12 months and 24 months postoperatively.[38] Some studies have reported that up to 40% endothelial cell loss can occur during the first 12 months and 4.2% annually thereafter for up to ten years after

PKP.[39] Whereas in DALK, 11% endothelial cell loss has been reported within the first six months which decreases to a rate of 1–2% annually, matching the physiological endothelial cell loss.[40] Peng et al recommend DALK in post-hydrops cases mainly due to the significantly greater endothelial protection.[41]

Refractive Outcome in PKP

In a retrospective study of 102 eyes with KC who underwent PKP, 31% of these patients had a history of resolved hydrops.[19] Long-term data regarding their visual outcomes included, more than 90% of patients with BCVA of 20/40 or better at all follow-up visits.[19] Additionally, their mean astigmatism decreased from 4.3 ± 2.6 D to 2.6 ± 0.9 D at one-year and five-years postoperatively.[19] The hydrops and non-hydrops groups exhibited similar refractive outcomes.[19] Similarly, a retrospective study of 211 eyes that underwent corneal transplantation concluded that the visual outcome in eyes with previous hydrops is equivalent to eyes without previous hydrops irrespective of the modality of corneal transplantation.[42]

Refractive Outcome in DALK

Table 1 presents the mean visual acuity of multiple publications that enrolled a total of 69 eyes that underwent varying methods of manual dissection for DALK. Post operatively, vision ranged from 20/25 to 20/47, and topographic astigmatism ranged from 3.14 D to 5.2 D (Table 1). These outcomes are comparable to those reported for PKP. Micro-perforations were reported in most of the studies and were successfully managed with intracameral gas injections without any visual sequelae.[12,25,28,43–45] Alharbi and Alameer evaluated 1288 cases that underwent DALK, and reported that 4 patients had DM perforations and were managed by fibrin glue.[44] They report good visual acuity that is comparable to DALK patients without perforations.[46] Similarly, Zhao et al reported that the mean BCVA was almost similar among eyes with DM scars irrespective of the involvement of the visual axis.[43]

Table 1 The Mean Reported Visual and Refractive Outcomes in Cases of Corneal Hydrops Managed by Deep Anterior Lamellar Keratoplasty in the Literature

Study	Eyes	Technique	Microper-Forations	Follow Up Period	Mean BCVA	Keratometric Corneal Astigmatism	Mean ECC
Zhao et al[43]	20 eyes	Manual blunt DALK dissection using a modified iris spatula with 'wet peeling technique' using hypotonic water. Leaving minimal corneal residual stroma.	2 cases (10%)	24 months	0.20 ± 0.11 logMAR	3.14 ± 1.25 Diopters	2021 ± 236 cells/mm^2
Ramam-urthi et al[25]	4 eyes	Modified DALK performed with controlled air injection to facilitate layer by layer stromal dissection up to 95% of its thickness with excision of DM incorporated in the scar followed by SF6 gas injection.	0	12 months	20/35	_	2044 cells/mm^2
Jacob et al[12]	9 eyes	Bevel –up needle insertion, creating tissue emphysema as a guide for dissection, using small aliquots of air opposite from the break followed by manual dissection leaving minimal stroma.	0	18 months (mean)	0.52 ± 0.13 Decimal	3.3 ± 1.63 Diopters	_

(*Continued*)

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Table 1 (Continued).

Study	Eyes	Technique	Microper-Forations	Follow Up Period	Mean BCVA	Keratometric Corneal Astigmatism	Mean ECC
Anwar & Anwar.[44]	22 eyes	Air injection at superficial to mid stromal depth followed by anterior keratectomy with multiple episodes of stromal hydration and air injection leaving a thin stromal layer.	6 patients	36 months	20/40	3.42 ± 1.7 Diopters	_
Goweid a et al[45]	12 eyes	Dissection of the peripheral stroma using the 'microbubble incision technique" to facilitate pre-DM stromal dissection. Followed by peeling the central posterior scar to bare DM.		12 months	0.38 ± 0.07 logMAR	5.2 ± 1.9 Diopters	2364 ± 316.8
Fuest & Mehta.[28]	2 eyes	One with a moderately steep cone and the other with a very steep cone. Both were treated with manual pre-DM dissection with a crescent blade with incorporation of sequential stromal hydration in the second case, baring the DM.	1 case	34 months	0.8 Decimal	_	2433 cells/mm^2

Abbreviations: BCVA, Best Corrected Visual Acuity; ECC, Endothelial cell count; KC, Keratoconus; DALK, Deep Anterior Lamellar Keratoplasty; DM, Descemet Membrane; SF6, Sulfur hexafluoride.

Visual Rehabilitation

The onset of suture removal after corneal transplantation surgery is an important indicator of visual rehabilitation. In DALK, suture removal can be performed within three to six months after the surgery. Whereas in PKP, sutures are usually removed after one year.[47] Earlier suture removal in DALK is attributed to its nature as a non-penetrating procedure. Therefore, overall ocular integrity, stability, and wound healing are believed to be better in DALK than in PKP.[28] In addition, early suture removal leads to earlier cessation of topical steroids. Halting topical steroids earlier can mitigate the risk of graft infiltrates related to loose sutures and other complications of prolonged use of steroids.[19] A meta-analysis has reported a 3X higher risk of high intraocular pressure and cataract in PKP compared to DALK.[48]

Conclusion

To summarize, the literature is scant regarding the outcome of DALK following healed hydrops compared to PKP. More studies are needed to address visual, refractive outcomes, and quality of vision in cases that have undergone DALK following healed hydrops. However, multiple studies have shown that the postoperative complications in DALK are lower compared to PKP. Therefore, considering DALK is advisable for KC following hydrops when feasible.

Ethical Approval

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

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Disclosure

None of the authors have competing interests in the material presented in this paper.

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