Review Article

Boston keratoprosthesis – Clinical outcomes with wider geographic use and expanding indications – A systematic review

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Abstract

Over 2 decades of research, several design modifications, and improvements in post-operative management have made Boston keratoprosthesis (B-KPro) a viable option for patients with corneal blindness for whom traditional keratoplasty procedure has a very low probability of success. In this systematic review, we examined the indications, visual outcomes, complications and retention rate of the literature published in the past 10 years (2005–2014). While most of the studies report smaller datasets (typically <50 eyes), some of the recent multicenter studies have reported large datasets (up to 300 eyes). Most of the literature is published from the US; however, last few years have witnessed some papers reporting the successful use of B-Kpro from developing countries or arid climatic conditions (such as the Kingdom of Saudi Arabia). Due to differences in the causes of corneal blindness in different geographic regions, newer indications for B-Kpro are emerging (e.g. trachoma). Additionally, improving clinical outcomes and increasing surgeon confidence have also expanded indications to include cases of unilateral visual impairment and paediatric age. We observed that there is growing body of evidence of successful clinical use of B-KPro; however, financial challenges, lack of trained surgeons, shortage of donor corneas must be overcome to improve accessibility of B-KPro.

Keywords: Boston keratoprosthesis, KPro, B-KPro, Keratoprosthesis implantation, Corneal transplantation

Introduction

Corneal diseases are the leading cause of blindness worldwide, second only to cataract.[1–3] While corneal transplantation is highly successful in restoring sight,[2] severely diseased eyes with deep corneal vascularization, limbal stem cell deficiency (LSCD), autoimmune diseases and chemical injury etc. are prone to graft rejection.[1,4] Keratoprosthesis (KPro) seems to offer visual rehabilitation in such situations where corneal transplantation has an extremely poor prognosis.[1,4] As of today, Boston keratoprosthesis (B-KPro) is the most commonly used KPro device worldwide. First case series of patients who had undergone type 1 B-KPro was reported in 1974, and the device was approved by the FDA in 1992.[5] Since its introduction, B-KPro has undergone

several design modifications, improving postoperative outcomes and surgeon confidence.

A review of literature reveals that most of the papers have been published from the US and reported smaller datasets (typically <50 eyes).[6–12] Recently, some of the papers from the US have reported large multicenter data set of up to 300 eyes.[13,14] With increasing accessibility of training programmes, last 4 years have witnessed several papers studying B-KPro implantation indications, complications and outcomes being published from regions across the world, particularly those from harsher climatic conditions (e.g. Jordan and Saudi Arabia in the Middle East) and from the developing countries (e.g. India, Nepal, Indonesia etc.).[5,12,15–17] Since the causes of corneal blindness necessitating B-KPro implantation vary with different geographical loca-

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tions and climatic conditions newer indications for B-KPro implantation (e.g. trachoma) are emerging. Similarly, the rate of post-operative complications and their management may vary with different geographical locations and climatic conditions.

At this time point, it is worthwhile to conduct a review of recent publications to examine the indications, visual outcomes, complications and retention rate of the B-Kpro literature published in the past 10 years, particularly of those from harsher climatic conditions (such as Saudi Arabia).

Systematic review – methodology

We searched the PUBMED on December 18, 2014 (no time limits) using relevant search terms such as *Boston keratoprosthesis, Boston KPro, B KPro* etc. and found 230 related publications. Additionally, Google search engine was searched for relevant literature. English language studies (reviews, case series and case reports) were included in the study. Results of English language publications published between 2005 and 2014 and reporting outcomes of 4 or more patients were reviewed and compared in Table 1. In this review, we discuss about common indications, postoperative outcomes including visual acuity, retention rate, complications of B-KPro and their management.

Keratoprosthesis: development history

The idea of replacing severely opacified cornea with artificial cornea (KPro) was first introduced by the French ophthalmologist, Guillaume Pellier de Quengsy way back in 1789. After the first report of successful implantation of a quartz crystal into the cornea was published in 1853,[4,18] attempts were made to refine KPro; however, high rate of failure with tissue necrosis, leakage, infection and extrusion of the device limited further developments. In the mean time, the first successful human to human corneal graft by Zirm in 1906 shifted the focus to keratoplasty and interest in KPro development decreased.[4] Gradually as the limitations of corneal transplantation came to fore, there was a renewed interest to develop KPro. KPro development received a major fillip after the high bio-compatibility of polymethylmethacrylate (PMMA) was learnt during World War II.[4]

Several different materials and designs have been proposed for KPro; some of the KPros are totally synthetic [e.g., B-KPro (also known as 'Dohlman–Doane' KPro) or AlphaCor] and the others are totally biological (e.g., tissue engineered cornea). Combined devices consisting of synthetic as well as biological material (e.g., Osteo-odonto KPro) are also available.[19] Of these, US Food and Drug Administration (FDA) approved KPros include B-KPro and AlphaCor.[20] With almost 200 peer-reviewed publications to date and with >6000 implantations performed worldwide until 2011, B-KPro is the most commonly used KPro in the United States and the rest of the world.[16,19,21,22]

B-KPro – description

B-KPro is a double-plated PMMA device with a central rigid optic that perforates the cornea. There are 2 variants of the device. Type 1, the more common variant, is a collar button-shaped device with front plate (diameter 5.5–7.0 mm),[20] a central optical stem, and a back plate (available in 8.5 mm diameter adult size and 7.0 mm diameter paediatric size),[23] with 8/16 holes that facilitate the nutrition and hydration of the corneal graft.[24,25] The back plate of the KPro is either screwed on to the stem to allow firm apposition with the donor tissue or snapped onto the stem with no rotating movement. A titanium locking ring is snapped in place behind the back plate to prevent loosening of the back plate. The graft prosthesis combination is then sutured to the recipient's trephined corneal opening as in penetrating keratoplasty. Type 1 B-KPro is available in a single standard pseudophakic power or customized aphakic optic allowing a maximum visual field of 60°.[20]

Type 2 B-KPro has a through-the-lid design with a 2 mm anterior nub designed to penetrate through a tarsorrhaphy and allow a visual field of 40°.[26] Type 2 is used in rare cases of symblepharon, extreme dry eyes, and other clinical sequelae associated with the autoimmune and inflammatory disease category that includes Stevens Johnson Syndrome (SJS) and Ocular Cicatricial Pemphigoid (OCP).

B-KPro – introduction and improvements over time

B-KPro was originally developed at the Massachusetts Eye and Ear Infirmary in the 1970s by Claes Dohlman as a collar button design made of PMMA consisting of a front plate, a stem, and a back plate.[20,22,27] Since the FDA approval in 1992 for marketing the device, several design changes and improvements in the post-operative management have helped reduce the postoperative complications and enhance the overall efficacy and safety of the procedure.[19,22,27,28]

The first significant improvement included replacement of the solid back plate with a back plate with holes. Addition of 16 round holes (1.17 mm diameter each) in the adult 8.5 mm sized back plate and 8 (1.3 mm diameter each) in the paediatric 7.0 mm sized back plate facilitated endothelial and keratocyte nutrition.[23,27,28] In addition, holes are also hypothesized to play a role in allowing the aqueous to replenish the fluid that has evaporated from the corneal surface, thus keeping the cornea hydrated and preventing dellen formation and dryness that could have lead to shrinkage, with subsequent leakage.[8]

In 2003, titanium locking ring was introduced to prevent any later intraocular unscrewing of the plates due to inadequate manual screwing.[19,27,28] However, this system still had several downfalls as manual screwing of the plates required rotation of the back plate which caused extensive damage to the posterior graft layers.[23] In order to prevent the carrier corneal graft from such damage and make the device easy to use, a newer design with threadless stem was introduced in 2007.[19,23] Incidentally, it also decreased the cost of manufacturing of the device as machining was replaced by moulding.[19]

The latest attempt to improve B-KPro outcomes has focused on exploring alternative materials. While PMMA is a transparent, biologically inert material with long history of safe intra-ocular use, several post-operative complications have been linked to the thick PMMA back plate.[28] Due to titanium's high resistance to corrosion, bio-inertness, ductility, lightness and strength[29] it can be easily machined

Table 1. Review of literature – summary of Indications, follow-up duration and outcomes of Boston keratoprosthesis.

Author/study	Country/region	Eyes	Time at last follow-up (FU)	CDVA preoperative		CDVA postop		Retention rate	Secondary KPro	Indications/preoperative diagnosis	Complications
				≥20/50	≥20/200	≥20/50	≥20/200				
Al Arfaj [42]	Saudi Arabia	16	>4 yrs	0%	0%	0%	69%	81.3%	50%	Trachoma (34.25%) Decompensated cornea post phacoemulsification (18.75%)	RPM[c] (50%) Worsened Glaucoma (18.8%) Vitreous haemorrhage (12.5%)
Lekhanont [45]	Thailand	42	4–5 yrs	0%	0%	NA~	43%	80.9%	59.5%	Corneal oedema (21.4%) Chemical injury (19.1%) Corneal dystrophies (19.1%)	Glaucoma/Elevated IOP (80.9%) RPM (52.4%) Corneal melt (23.8%)
Srikumaran [46]	USA	139	6 wks–8.7 yrs	NA~	10.8%	NA~	70%	67%	73%	Bullous keratopathy (35.3%) Ocular Surface Disease (23%) Congenital Corneal abnormalities (12.9%)	RPM (49.7%) Glaucoma/Elevated IOP (36.2%) Sterile corneal necrosis (19.5%)
De Oliveira [43]	Brazil	30	1–55 months	0%	0%	NA~	80%	93.3%	53.3%	Chemical injury (33.33%) SJS (13.33%)	Worsened Glaucoma (43%) RPM (26.66%) Corneal melt (20%)
Phillips [47]	USA	9	29–60 months	0%	11.11%	44.4%	22.2%	77.8%	88.9%	Chemical/Thermal burns (100%)	Cyclitic membrane/RPM (22.2%) Microbial keratitis (22.2%) Sterile corneal ulceration (22.2%)
Hassanaly [48]	Canada	26	4–50 months	0%	0%	0%	54%	77%	27%	Aniridia (100%)	Glaucoma (88%) RPM (58%) Vitritis (26.1%)
Brown [49]	USA	9	22–63 months	0%	22.2%	11.1%[a]	66.7%	66.7%	88.9%	Herpes simplex virus (55.6%) Herpes zoster virus (44.4%)	Epiretinal membrane (66.7%) RPM (44.4%) Microbial keratitis (33.3%)
de la Paz [22]	Europe	67	3 yrs	NA~	NA~	NA~	NA~	78%	83%[b]	Autoimmune (24%) Chemical/Thermal burns (18%) Leukoma post Infectious Keratitis (10.5%)	RPM (34%) New/worsened Glaucoma (24%) Retinal/choroidal detachment (19%) Endophthalmitis (13%)
Jasinskas [17]	Lithuania	5	3–5 yrs	0%	0%	60%	100%	100%	60%	Chemical injury (20%) Thermal injury (20%)	RPM (40%) Elevated IOP[d] (100%) Secondary cataract formation (40%)
Ciolino [50]	USA	300	1 wk–>6.1 yrs	NA~	NA~	NA~	NA~	93%	86.2%	Bullous keratopathy (18.3%) Autoimmune (10.3%) Chemical injury (10.3%)	RPM (1%)[e] Infectious keratitis (6.3%)[e] Sterile corneal necrosis (1.7%)[e]
Shihadeh [5]	Jordan	20	3–36 months	0%	0%	25%	65%	90%	95%	Corneal vascularization (40%) Keratoconus (20%)	RPM (45%) New/worsened glaucoma (20%) Infectious keratitis (10%)
Al Arfaj [15]	Saudi Arabia	4	6–14 months	0%	0%	25%	100%	75%	25%	Trachoma (50%) Chemical injury (25%)	PED[f] (25%) Prosthesis edge melts (25%)
Rudinsky [32]	USA	265	146 eyes (≥1 yr FU), 87 eyes (≥2 yrs FU)	NA~	NA~	NA~	NA~	NA~	85.4%	Bullous keratopathy (15.5%) Chemical injury (9.1%)	RPM (31.7%)

Study	Country	N	Follow-up							Indication	Complications
Aldave [16]	Armenia, India, Indonesia, Nepal, Philippines, Russia, Saudi Arabia	107	<1.0–48 months	0%	1%	18%[g]	41%[g]	81%	44%	Chemical injury (27%)	RPM (27%)
										SJS[h] (8%)	Sterile Corneal Necrosis (18%) Elevated IOP (14%)
	USA	98	<1.0–84 months	0%	6%	16%[i]	29%[i]	80%	64%	Repeat KPro (12%) Chemical injury (7%)	RPM (46%) PED (34%) Elevated IOP (19%)
Patel [41]	USA	58	3–47 months	NA~	2%	NA~	43%	78%	81%	Infectious keratitis (19 %) LSCD[j]/Bullous keratopathy (17%)	RPM (50%) Elevated IOP (25.9%) Prosthetic melt (25%)
Greiner [11]	USA	40	≥1 year	0%	5%	48%	50%	80%	47.5%	Chemical injury (25%) Aniridia (12.5%)	RPM (55%) Elevated IOP (40%) Glaucoma: New (27.5%) Worsened (22.5%)
Robert [12]	Canada	47	3–18.5 months	NA~	≥6%	≥11%	NA~	100%	57%	Aniridia (34%) Bullous keratopathy (11%)	Elevated IOP (51%) RPM (26%) New/worsened glaucoma (21%)
Sejpal (LSCD) [35]	USA	23	0.5–58.6 months	0%	4%	30%[i]	30%[i]	74%	NA~	LSCD (100%)	PED (56.5%)
										Chemical injury (30.4%) SJS (26.1%)	Sterile corneal necrosis (30.4%) RPM (26.1%)
Sejpal (non-LSCD) [35]	USA	56	0.5–58.6 months	0%	9%	5%[i]	20%[i]	82%	NA~	NA~	RPM (46.4%)
											PED (23.2%) Elevated IOP (17.9%)
Verdejo-Gomez [51]	Spain	12	23 months (mean FU)	0%	0%	8%	17%	100%	92%	Herpes keratitis (8%)	Corneal thinning (33%)
											Glaucoma progression (8%)
Chew [10]	USA	37	6–28 months	0%	14%	43%	81%	100% in type 1[k]	59%	Bullous keratopathy (42%) Aniridia (11%)	RPM (67%) Elevated IOP (39%) Glaucoma (14%)
Bradley [9]	USA	30	1 yr	0%	13%	>23%	75%	83.30%	87%	Chemical injury (10%) SJS (3%)	RPM (43%) Elevated IOP (27%) Infectious keratitis (17%) Corneal Melt (17%)
Aldave [34]	USA	50	4 yrs	0%	10%	NA~	100%	84%	84%	LSCD (28%) Chemical injury (10%)	RPM (44%) PED (38%) Elevated IOP (18%)
Sayegh [8]	USA	16	10.2 months–5.6 yrs	0%	0%	31%	50%	NA~	NA~	SJS (100%)	RPM (56.5%) Skin retraction (Type 2) (25%) Retinal detachment (12.5%)
Akpek [7]	USA	16	2–85 months	0%	0%	0%	63%	100%	68.75%	Aniridia (100%)	RPM (12.5%) Choroidal detachment (12.5%)

Table 1 (continued)

Author/study	Country/region	Eyes	Time at last follow-up (FU)	CDVA preoperative ≥20/50	CDVA preoperative ≥20/200	CDVA postop ≥20/50	CDVA postop ≥20/200	Retention rate	Secondary KPro	Indications/preoperative diagnosis	Complications
Zerbe [31]	USA	136	At least 1 year	0%	4%	32.2%	56.40%	95%	54%	Chemical injury (15%), Herpetic keratitis (7%)	RPM (26%), Elevated IOP (15%), Sterile vitritis (5%)
Aquavella [6]	USA	25	2–12 months	0%	0%	20%	24%	100%	88%	Corneal vascularization (4%), Band Keratopathy (4%), Bullous Keratopathy (4%)	RPM (12%)

NA^(Not Available) – Either the respective values were not reported or the values were reported in other formats in those studies For e.g., median visual acuity (logMAR) values.
a The value indicates percentage of eyes with ≥ 20/40 visual acuity (the value for ≥ 20/50 was not available).
b The value calculated as percentage of patients instead of percentage of eyes.
c RPM (Retroprosthetic Membrane).
d IOP (intraocular pressure).
e Complications reported in cases of keratoprosthesis failure.
f PED (Persistent Epithelial Defect).
g CDVA reported at 1 year, which approximates the mean FU time.
h SJS (Steven's Johnson Syndrome).
i CDVA reported at 2 year, which approximates the mean FU time.
j LSCD (limbal stem cell deficiency).
k One eye with type 2 failed at 9 months in this study.

into thin, flexible, larger diameter plates (which are resilient to stress),[6,11] potentially reducing the incidence of post operative complications such as anterior iris synechiae and angle closure glaucoma,[27,30] particularly in uveitis or sterile vitritis cases. Todani et al. investigated the clinical outcomes of combining the transparent PMMA stem and front plate with titanium back plate and reported the decline in rate of retroprosthetic membrane (RPM) formation from 46.1% in eyes implanted with threaded PMMA to 31.2% with thread-less PMMA to 13% in threadless titanium backplates.[31]

Clinical outcomes

Type 1 B-KPro

Indications

The B-KPro is indicated for patients with refractory corneal blindness and having extremely poor prognosis for penetrating keratoplasty. A review of literature revealed that secondary keratoprosthetic implantation (KPro implantation attempted after failed corneal graft) accounted for majority of the cases, as high as 95% of the procedures in a study from Jordan, followed by 88% and 87% in two studies from the United States (Table 1).[5,6,9] The two large data set multicenter studies involving up to 300 eyes also reported failed corneal graft to be the most common indication (85–86%).[32,33]

Literature review also seems to suggest that indication of primary B-KPro implantation (KPro implantation performed without first attempting keratoplasty) included eyes with severe ocular surface damage due to chemical or thermal injury (percentages varying from 7% to 30.4% in different studies) (Table 1)[9,11,15–17,31–35] or autoimmune diseases such as SJS (2.5–100%)[8–11,16,34,35] or congenital anomalies such as aniridia (1–100%).[12,17,23,34–37] While bullous keratopathy and aniridia were reported commonly in the studies from the US and Canada, post-trachomatous scarring[15] was the most common indication from Saudi Arabia (Fig. 1) and chemical injury was the common indication internationally.[7,12,13,16,17,20,23,34,38] Thus the indications for B-Kpro from different geographical regions vary due to differences in the causes of corneal blindness. Further, advances in post-operative outcomes, reducing rate of complications,[27] and increasing surgeon confidence have also expanded indications and reduced contra-indications. Unilateral visual impairment, which was once considered a strong relative contraindication due to high risks associated with KPro implantation, is no longer considered so, as some studies have reported good visual outcomes with restoration of binocularity.[34,36,37] B-KPro has also been successfully implanted in paediatric eyes.[39,40] Since traditional penetrating keratoplasty in children has poor prognosis due to their robust immune response, typically resulting in prolonged recovery time and neovascularization extending into the visual axis successful B-KPro implantation may prevent stimulus deprivation amblyopia.[40] It is being hypothesized that, after successfully preventing amblyopia, keratoprosthesis may be exchanged for a traditional corneal transplant later in life.[39]

Visual outcomes

Most of the studies reported pre-operative visual acuity of worse than 20/200 in majority of the eyes. Post-operatively, visual acuity improved significantly with majority of the stud-
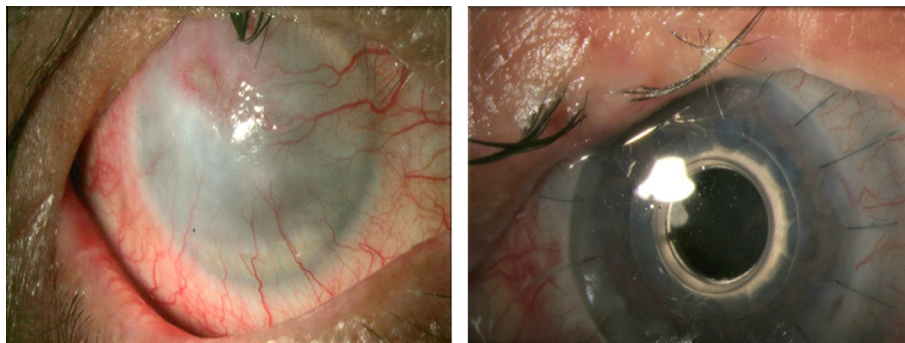
Figure 1. (A) Pre-operative clinical photograph of the right eye of a patient with post-trachomatous corneal scarring showing deep vascularization in all 4 quadrants. (B) Post-operative clinical photograph of patient 6 months after B-KPro implantation.

ies reporting more than 50% of the eyes achieving CDVA of 20/200 or better (Table 1). While several studies reported achieving CDVA of 20/50 or better in at least some of the eyes 4 papers reported achieving CDVA of 20/50 or better in 43–60% of their dataset.[10,11,17,41] Visual acuity in case series from arid climatic conditions of Saudi Arabia and Jordan also reported good visual outcomes with 65–100% of the eyes achieving CDVA of 20/200 or better and 0–25% of the eyes achieving visual acuity of 20/50 or better[5,15,42] which are comparable to those from the US (with 20–81% of the eyes achieving CDVA of 20/200 or better and 0–48% of the eyes achieving CDVA of 20/50 or better).

Retention rate

Overall, between 74% and 100% of B-KPro were reported as retained at the last follow-up (range 1 week to 85 months, Table 1). The longest reported retention time (of at least one patient in a 16 cases report by Akpek et al.) is 85 months.[7] Retention rate of 100% has been reported in 5 publications containing data of 5–47 eyes (3 from the US, 1 from Canada and 1 from Lithuania).[6,7,10,12,17] Even in the studies reporting larger dataset (136–300 eyes), retention rate of 93–95% is obtained.[31,38] Case series from Saudi Arabia and Jordan have also reported good retention rates (75–100%)[5,15,42]; it is important to note that despite the arid climate of this region, which contributes to the ocular surface dryness, the retention rate reported in this study is consistent with the reports from other parts of the world.

The expected outcomes seemed to be influenced by the primary indications. Apparently, best results were observed in non-cicatrizing conditions and preoperative conditions such as autoimmune diseases, chemical injury, LSCD, deep corneal vascularization were found to be associated with studies reporting lower retention rates.[11,15,16,22,34,35] Similarly, complications such as persistent epithelial defect (PED), corneal necrosis and endophthalmitis seemed to be more common in case series reporting comparatively lower retention rates.[15,16,22,35]

While elevated intraocular pressure (IOP) (14–100% eyes) and glaucoma (2–43% eyes) were a common complication, it did not seem to affect the retention rates.[5,12,17,43,44] As such, RPM was the most commonly reported complication (affecting between 12% and 67% eyes). Other common complications included PED (23–56.5%), infectious keratitis (6.3–17%), sterile corneal necrosis, Retinal/choroidal detachment, prosthetic melt, endophthalmitis, secondary cataract and sterile vitritis (Table 1).

Type 2 B-KPro

There is limited literature on the outcomes of type 2 B-KPro, a total of 11 eyes compared to approximately 1400 eyes of type 1 B-KPro. Sayegh et al. reported data of 16 B-KPro implantations in SJS affected eyes out of which 10 had undergone type 2.[39] Complications were reported for all the 16 eyes; separate statistics are not available for B-KPro type 2. Chew et al. reported data of 36 type 1 B-KPro and one type 2 B-KPro for a case of OCP while retention rate was 100% for type 1 (6–28 months follow-up), type 2 got extruded after 9 months of follow-up.[37]

Post-operative complications – prevention and therapeutics

Over the decades, improvements in the postoperative management have contributed to the improvement of KPro's clinical outcomes.

Ocular surface dryness

Managing ocular surface dryness is one of the most significant challenges in the post-operative care of B-KPro as it may cause dellen formation and ulceration.[27,28] Bandage contact lenses have been found to significantly improve ocular surface health and stability, reducing the incidence of dryness associated complications. In addition to its protective and therapeutic roles, bandage contact lens after KPro surgery also improves cosmesis and allows refractive adjustments (it is possible to customize the bandage contact lenses to offer refractive correction).[52] While bandage contact lenses are advantageous in improving ocular surface health, it is important to regularly clean and if needed replace them, so that they do not serve as foci of infection.[53]

Endophthalmitis

Due to the very nature of the procedure, in which a non-biointegrating material replaces the entire thickness of the central cornea as eye's outer most layer, B-KPro carries a long term risk of infection. Literature review revealed endophthalmitis prevalence rate of 0-13% in patients implanted with

B-KPro.[5,9–11,16,22,33,41,53] In order to prevent potentially sight threatening post-operative infections such as endophthalmitis,[53] the use of prophylactic antibiotics is recommended. In particular, the use of vancomycin has reduced the incidence of infectious endophthalmitis in autoimmune patients as well.[27,28] Concurrent use of vancomycin or chloramphenicol along with fluoroquinolones is recommended in high risk patients after B-KPro as preventive measures.[53–55] However, vancomycin must be specially prepared and chloramphenicol is not commercially available in some countries for e.g., the US.[55] While the chronic use of low-dose antibiotics may help decrease the risk of infection, it may, to the contrary, increase the risk of inducing resistance among ocular flora. There are suggestions that increase in dosage from 2 times to 4 times per day may possibly prevent such development of resistance.[10]

Patients with autoimmune disease and chemical burns are more vulnerable to endophthalmitis development.[53] Regular cleaning and replacement of therapeutic contact lens are also recommended to remove the bulk of infecting colonies.[53]

Retroprosthetic membrane

RPM is one of the most common complications (affecting 12–67% of eyes) after B-KPro.[10,11,16,17,22,31,32] According to a recent multicenter study, B-KPro implantation in eyes with corneal blindness due to infectious keratitis and aniridia is at the highest risk of RPM development.[33] In contrast, chemical injury seems to be protective against RPM development with only one-third of these patients developing RPM after a longer time period.[32] In most cases, Nd:YAG laser membranectomy can effectively treat RPM before it becomes too thick and vascularized.[20,27,28]

Elevated IOP and glaucoma

One of the most difficult complications to be managed after KPro is glaucoma.[13] As such, eyes that need KPro implantation are severely diseased with most of them either already having glaucoma or being highly vulnerable to developing glaucoma.[56] A review of literature reveals that after B-KPro implantation, incidence of elevated IOP is 14–100%[9–11,16,31,34,35,41] and that of new or worsened glaucoma is 2–43% of the eyes in the US as well as Middle East region.[5,7–12,16,22,34,43,44]

A recent publication reporting anterior segment OCT findings of the B-KPro implanted eyes revealed that early anatomic changes related to glaucoma progression (anatomic angle narrowing and synechiae progression) were present in almost all eyes (including eyes with no previous history of glaucoma or increased IOP), suggesting that there is a long term risk of almost all eyes progressing to glaucoma.[44] Therefore, all B-KPro implanted patients should be followed up closely, so as to diagnose and manage raised IOL early on[14]; however, IOP monitoring in these patients remains challenging as there are no reliable tools to assess IOP in B-KPro implanted eyes and therefore clinician's reliance on the subjective digital palpation to monitor IOP.[13,57] IOP can be controlled by surgical placement of glaucoma drainage device, but the procedure itself may cause several complications.[13]

Endoscopic or transscleral diode cyclophotocoagulation or pars plana tube insertion may be attempted when previously placed glaucoma drainage devices are not adequately functioning.[57] Pars plana tube insertion with concomitant pars plana vitrectomy may be a viable alternative treatment that can avoid occlusion secondary to anterior segment crowding or to vitreous and iris plugging. In addition, the vitrectomy offers the ability to clear any vitreous opacities or RPM that may be obstructing vision.[57]

Corneal melt

The incidence of corneal melt as reported in the literature is also high (1.5–17%).[7–9,11,31,58] Although keratoprosthesis design with 8[59] (and now 16) backplate holes has lowered the incidence of corneal melt from 51% to 10%, the risk of developing corneal melt in high-risk patients can be further minimized by using bandage contact lens which improves corneal hydration and thus prevents dellen formation and melting.[10] The management of corneal melt is usually done by optimization of the tear film (with artificial tears and punctual occlusion), resuturing, cyanoacrylate glue application and use of anti-collagenolytic agents, such as topical medroxyprogesterone and oral tetracyclines.[60,61] In addition, surgical measures such as tutoplast patch graft, conjunctival flap, buccal mucosal graft, lateral tarsorrhaphy, donor corneal lamellar graft or crescentic amniotic membrane grafting can be performed in severe cases.[61] Eyes with corneal melt and concomitant active autoimmune disease may benefit from the administration of systemic immunosuppressives. In refractory cases, the device may be explanted and replaced with another keratoprosthesis or managed with regraft.[61]

Vitreoretinal diseases

Vitreoretinal complications after B-KPro implantation, specifically retinal detachment have been reported in 5–19% of the eyes.[7,8,12,16,22,31,34,35,41] Such complications usually require surgical management by pars plana vitrectomy, which reportedly can be performed successfully in B-KPro implanted eyes. While such vitreo-retinal procedures have yielded good anatomical outcomes, visual recovery has not been commensurate, typically offering little improvement in visual acuity.[62,63]

Improving outcomes – future developments

Literature published to date indicates promising results of B-KPro implantation; however, there are several facets of B-KPro design, implantation and post-operative care that need continued innovation and development.

IOP measurement devices

Prevention of glaucoma after B-KPro surgery is a major priority at the time of KPro evaluation and during postoperative follow-up. Due to the rigidity of the large B-KPro back plate in B-KPro–implanted patients (with preoperative glaucoma), it is difficult to accurately measure IOP by means of standard tonometers.[56] Therefore, there is a need to develop innovative IOP measurement devices. Telemetric IOP measurement is one such technique, which allows monitoring of IOP in patients with keratoprosthesis whose IOP cannot be

measured by current methods. A recent experimental study of telemetric IOP records used a wireless transducer implanted in rabbits after extracapsular lens extraction demonstrating concordance with direct manometry measures.[64] Further studies are necessary, however, to validate its use and safety in human eyes.

Retro-backplate membrane thickness and risk of melt

While the recent B-KPro model having 16 backplate holes has substantially reduced the risk of corneal melt, it still occurs in 1.4–17% of the surgeries.[11,31,34] It has been postulated that the formation of a retro-backplate membrane in B-KPro patients predisposes patients to melt (sterile keratolysis) because of the resultant occlusion of backplate holes and impedance of nutritional support from the aqueous humour.[58] However, the newer large diameter titanium backplate B-KPro design may offer greater protection from RPM formation than the older PMMA backplate model.[29] Further studies with the new titanium backplate B-KPro may evaluate the incidence of RPM formation and the role they play in melt pathogenesis.[58]

Prevention of infectious keratitis and endophthalmitis after KPro implantation

Infectious keratitis, corneal melts and endophthalmitis are inter-related problems that may result in devastating consequences after KPro surgery.[65] While the management of endophthalmitis after KPro implantation has improved, post-KPro endophthalmitis continues to have higher incidence, early onset and extremely poor visual outcome compared with other intraocular surgeries.[66] Since the aetiology of post-KPro endophthalmitis may include both bacterial and fungal infections,[66] therapeutic dosing of topical antibiotics and antifungal agents, rather than the chronic low-dose prophylaxis antibiotics currently used after KPro surgery, may possibly prevent the development of resistant organisms.[53,54] Alternatively, the use of antibiotic-coated prostheses or antibiotic-secreting contact lenses has been proposed and is under active investigation.[60,67] A recent publication explored the use of high-fluence collagen crosslinking (CXL) as a means of achieving increased corneal rigidity and reduced enzymatic digestion in the vehicle cornea of 11 B-KPro eyes and reported no corneal melts and/or infection over a mean follow up of 7.5 years (range 1–9 years)[68]; the results seem very promising and future studies may validate the reproducibility of outcomes under different clinical settings.

Keratoprosthesis in autoimmune diseases

The KPro surgery has enjoyed high success rates, particularly in the category of nonautoimmune patients; however, in patients with inflammatory autoimmune diseases,[60] continued innovations and clinical trials are needed. Studies are needed to assess the clinical importance of commensal organisms on the ocular surface of KPro patients, and for potential inflammatory responses to the materials contained in the KPro.[60] With improved understanding of the underlying disease mechanisms in autoimmune disorders, in future more directed treatments for patients needing KPro for autoimmune corneal blindness may be achieved.

Although, patients with autoimmune diseases such as SJS usually have a poor long term prognosis of Kpro implantation, the retention rate and visual outcomes of the prosthesis implantation can be improved by regular systemic autoimmune therapy such as monthly infliximab infusions.[69] Further studies are required to assess the effect of systemic autoimmune therapy on prosthesis retention and visual outcomes in other autoimmune diseases.

Enhancing accessibility

While continued research and innovation are indispensable to improve B-KPro's design and material and decrease associated complications, efforts must also be made to enhance its accessibility. Majority of people with corneal blindness needing surgical rehabilitation live in the developing countries where training programmes in B-KPro implantation are not available, donor corneal tissue is scarce and recipients cannot afford the cost of KPro surgery and postoperative care.[1,21] It is, therefore, important that the formal training programmes in B-KPro implantation, that are currently offered in only a few countries, be made available to the surgeons all over the world; it may increase the accessibility of KPro to a lot more patients in need.[1] Additionally, there is a need to find alternative carrier tissue that must be inexpensive, readily available, and safe so that scarcity of corneal tissue does not limit the utility of B-KPro. Available data on the use of cryo-preserved and gamma-irradiated carrier corneas seem promising; visual acuity outcomes, incidence of complications, and retention percentage of the KPro implantations with preserved carrier corneas have been found to be comparable to those with fresh carrier corneas.[70,71] While B-KPro is already being made available at subsidized rates in developing countries, increasing use of B-KPro may facilitate economy of scale in production, potentially further decreasing costs.

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