Clinical Research 

# Clinical manifestation and management of severe blepharokeratoconjunctivitis combined with corneal perforation

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## Abstract

• **AIM:** To investigate the clinical signs of blepharokeratoconjunctivitis (BKC) and evaluate the efficacy of penetrating keratoplasty (PKP) for the disease.

• **METHODS:** Sixteen patients (16 eyes) with BKC complicated by corneal perforation hospitalised at Shandong Eye Hospital were retrospectively analyzed. All patients received PKP. Participants were assessed for symptoms, clinical manifestations, the activity and damage grading of BKC. A paired *t*-test was used to compare the uncorrected visual acuity (UCVA) before and after surgery for the perforated eye.

• **RESULTS:** The mean age of the patients was 16.3y. Blurred vision is the most common discomfort, followed by redness, and then photophobia. The duration of ocular discomfort lasted for 3.2y, on average. Three (18.8%) participants were associated with rosacea, while 11 (68.8%) patients had recurrent chalazion or hordeolum. *Demodex* in eyelash follicles was positive in 11 (68.8%) cases. All corneal perforations were  $\leq$ 3.0 mm in diameter. The perforation was located mainly in the inferior cornea (68.8%). The mean area of corneal vascularisation was 3.0 quadrants. All patients manifested bilateral BKC, with the perforated eyes ranked as severely damaged and presenting with severe inflammation. Most contralateral eyes manifested mild damage with no active inflammation. Majority (68.8%) of the perforated eyes were treated with PKP using a minimal graft. The UCVA increased significantly at the final follow-up (mean, 21mo; P<0.001), with the manifestation of BKC alleviated greatly. None of the patients developed immune rejection or other serious complications.

• **CONCLUSION:** BKC combined with corneal perforation occurs mainly among young people with a long history of ocular discomfort. PKP, especially using a minimal graft, is an effective and safe option for treating the disease.

• **KEYWORDS:** blepharokeratoconjunctivitis; corneal perforation; penetrating keratoplasty

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### INTRODUCTION

**B** lepharitis is classified as anterior blepharitis and posterior blepharitis. The former involves the eyelid skin up to the lash base and follicles, while the latter involves the meibomian glands<sup>[1]</sup>. Blepharitis affects up to 47% of ophthalmology patients, causing recurrent chalazion or hordeolum<sup>[2]</sup>. Blepharokeratoconjunctivitis (BKC) is an ocular surface disease involving disorders of the eyelids, dysfunction of the meibomian glands and inflammation of the conjunctiva and cornea<sup>[3]</sup>. Although BKC may cause ocular symptoms, such as redness, tearing, photophobia, itching and pain, it is often overlooked and misdiagnosed because of its divergent presentation<sup>[4-5]</sup>.

BKC is estimated to account for 15% of paediatric eye disorders<sup>[6]</sup>. When onset is at an early age, BKC has the potential to lead to sight-threatening complications, such as amblyopia, corneal opacity and corneal neovascularisation. BKC may also be associated with skin-related diseases, such as rosacea<sup>[7-10]</sup>. BKC combined with corneal perforation is an

extremely rare complication that has not yet been sufficiently explored. Hamada *et al*<sup>[11]</sup> reported a severe phenotype of BKC with duration of the ocular disorder persisting into early adulthood, with a high risk of corneal complications, including two cases of corneal perforation. Medsinge *et al*<sup>[12]</sup> assessed the outcome of penetrating keratoplasty (PKP) for treating one case of BKC-combined corneal perforation.

Wearing a contact lens or gluing the cornea to cure a small corneal perforation is not applicable to treating BKC combined with perforation<sup>[13-15]</sup>. Moreover, conservative treatment frequently results in severe corneal scarring and high irregular astigmatism in these patients<sup>[16]</sup>. Because severe BKC commonly presents with extensive corneal vascularisation, it has been considered that graft failure and rejection risk might increase in corneal transplantation on a vascularised bed<sup>[17-18]</sup>. Nevertheless, in this study, we assessed 16 cases of BKC complicated by corneal perforation, who were treated successfully by PKP surgery combined with medication and physiotherapy. This article evaluates the clinical characteristics and therapeutic efficiency of BKC complicated by corneal perforation and highlights the importance of early diagnosis and intervention in the disease.

#### PARTICIPANTS AND METHODS

**Ethical Approval** The study was approved by the Ethics Committee of Shandong Eye Hospital (Ethics No.BKC combined with corneal perforation, SDSYKYY 202201-01) and adhered to the tenets of the Declaration of Helsinki. Written informed consent was obtained from all participants.

**Research Participants** Patients diagnosed with BKC combined with corneal perforation who were hospitalised in Shandong Eye Hospital between January 2015 and December 2022 were included in the study. The diagnostic criteria of BKC are based on recurrent episodes of chronic red eye, changes in the lid margin (telangiectasia, thickening and scarring), blepharitis and chalazion or hordeolum, accompanied by keratitis (corneal punctate erosion, punctate keratitis, infiltration, opacities, ulceration, thinning, vascularisation, scar formation and perforation)<sup>[19-21]</sup>. The inclusion and exclusion criteria are as follows:

Inclusion criteria: 1) eyes diagnosed with BKC; 2) eyes complicated by corneal perforation.

Exclusion criteria: 1) microbial infections; 2) history of eye surgery; 3) history of eye trauma; 4) history of atopic blepharitis or keratoconjunctivitis; 5) history of perennial allergic conjunctivitis; 6) history of vernal keratoconjunctivitis; 7) history of herpetic keratitis; 8) lactating or pregnant women. **Clinical Information** The eyelid, lid margin, conjunctival and corneal status were assessed using slit-lamp biomicroscopy. Intraocular inflammation was evaluated using an ocular B-ultrasound. The structures of the cornea and anterior chamber were assessed by anterior segment optical coherence tomography (AS-OCT; Optovue, RTVue100-2, Fremont, CA, USA). Eyelash infestation with *Demodex folliculorum* was estimated by *in vivo* confocal microscopy (HRT3; Heidelberg Engineering, Dossenheim, Germany)<sup>[22]</sup>. Data were collected before and after surgery, including demographic information, ocular surface characteristics, uncorrected visual acuity (UCVA), intraocular pressure (IOP) and postoperative outcomes.

**Symptom Evaluation** The subjective symptoms of BKC<sup>[23]</sup>, including redness, tearing, blurred vision, pain, irritation, photophobia, white spots, swelling, discharge, itching and rubbing, were evaluated at the patients' presentation at hospital and during follow-up.

Activity and Damage Grading of BKC The ocular surface disorders of BKC were graded based on bimodular activity and the degree of damage, as previously reported<sup>[11]</sup>. The grades of disease activity ranged from A0 (no active inflammation) to A3 (severe inflammation), based on conjunctival hyperemia/ oedema, corneal vascularisation, conjunctival or corneal ulceration, or corneal perforation. The grade of disease damage ranged from D0 (no damage) to D3 (severe residual damage), based on lid distortion, subconjunctival fibrosis, the presence and extent of established vessels/fibrovascular pannus, and peripheral/central corneal thinning.

**Surgical Technique** During surgery for the peripheral perforation, if the central cornea was transparent, PKP with a minimal graft was performed, as described previously<sup>[24]</sup>. For central corneal perforation or peripheral perforation accompanied by extensive corneal opacity or neovascularisation, conventional PKP (orthokeratoplasty with a graft diameter of 7.5–8.0 mm) was conducted, and the surgical procedure was like standard PKP<sup>[25]</sup>.

**Medication Intervention and Adjuvant Therapy** For the perforated eye, 0.5% levofloxacin eye drops (Santen, Osaka, Japan) and intravenous antibiotics were administered to prevent infection. Postoperatively, ofloxacin eye ointment was applied four times daily and then replaced with topical antibiotic eye drops. Tobramycin and dexamethasone eye ointment (Alcon Cusi S.A, Masnou, Barcelona) were administered two times per day for five to seven days and then replaced with 0.1% or 0.02% fluorometholone eye drops (Santen, Osaka, Japan). Tacrolimus eye drops (Senju, Fukusaki Plant, Japan) or 1% Cyclosporin A (CsA) eye drops (North China Pharmaceutical Co., Ltd) were administered and tapered gradually<sup>[26]</sup>. Artificial tear eye drops were applied based on the ocular surface status.

For the contralateral eyes, if they manifested with no active inflammation and no damage, artificial tear eye drops were applied. For the eyes with corneal infiltration and opacity, 0.1%

or 0.02% fluorometholone eye drops and topical antibiotic eye drops were added. Besides, if the eyes accompanied by extensive corneal neovascularisation, Tacrolimus eye drops or 1% CsA eye drops were given.

After surgery, lid margin cleaning was performed daily for the both eyes. Tea tree oil cleaning wipes (OCuSOFT, Inc., US) were used to treat *Demodex* blepharitis. Oral azithromycin was administered for severe meibomian gland dysfunction (MGD). Warm lid compresses or intense pulsed light (IPL) therapy were administered one month postoperatively. IPL therapy at an interval of three weeks was performed for severe blepharitis or MGD. Patients were examined daily in the first week, monthly in the first year, and four to six times per year thereafter.

Statistical Analysis Measurement data were expressed as mean±standard deviation (SD). Categorical data and ranked data were expressed in frequencies and percentages. The Shapiro-Wilk test was applied to check the normality of the measurement data. A paired *t*-test was used to compare UCVA before and after surgery. SPSS version 22.0 was used for the statistical analysis, where a *P* value of <0.05 was considered statistically significant.

#### RESULTS

**Characteristics of the Subjects** Sixteen participants (16 eyes) were included in the study, including 13 females and 3 males, with a mean age of  $16.3\pm5.9y$  (range 9–35y). The average age of BKC onset was 13.1y. The average time from symptom onset to presentation at the hospital for treating corneal perforation was  $3.2\pm3.4y$  (range 0.25-15y).

Among these patients, the majority (87.5%) had received medication treatment previously, but most of these patients were misdiagnosed as herpetic keratitis, and long term antiviral eyedrops have exacerbated damage to the ocular surface. Three (18.8%) participants were associated with rosacea, while 11 (68.8%) patients had recurrent chalazion or hordeolum. *Demodex* eyelash infestation was positive in 11 (68.8%) patients (Table 1).

Ocular Surface Features of the Subjects The evaluation of ocular surface signs revealed common characteristics. BKC-combined corneal perforation showed severe corneal vascularisation, with an average neovascularisation area of  $3.0\pm1.0$  quadrants (range 1–4 quadrants). The perforations were located mainly at the inferior cornea (11, 68.8%), including perforation in the infranasal region in four eyes, the infratemporal area in three eyes, located at the inferior peripheral cornea in two eyes (6 o'clock position), and involving the inferior pupillary zone in two eyes. In addition, perforation occupied the nasal peripheral cornea in two eyes (3 or 9 o'clock positions) and involved the central cornea in three eyes (Table 1).

# Table 1 Clinical information and ocular surface disorders of the study subjects

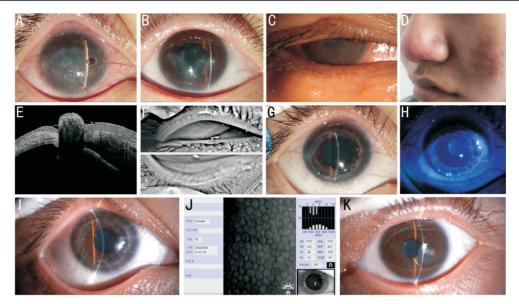
Characteristics	Data
Subjects (eyes), n	16
Age (y), mean±SD (range)	16.3±5.9 (9.0–35.0)
Gender (M:F)	13:3
Duration of ocular discomfort (y), mean±SD (range)	3.2±3.4 (0.25–15.0)
Rosacea (yes/no), n	3/13
Recurrent chalazion or hordeolum (yes/no), n	11/5
Demodex in eyelashes (positive/negative), n	11/5
Corneal neovascularisation area (quadrants), mean±SD (range)	3.0±1.0 (1-4)
Diameter of corneal perforation, n	
1.0 mm	4
1.5 mm	4
2.0 mm	1
2.5 mm	3
3.0 mm	4
Location of corneal perforation, n	
Infranasal region	4
Infratemporal region	3
Inferior peripheral region (6 o'clock position)	2
Inferior pupillary zone	2
Nasal peripheral region (3 or 9 o'clock position)	2
Central region	3

SD: Standard deviation.

Most perforations presented with a small diameter, including 1.0 mm in four eyes, 1.5 mm in four eyes, 2.0 mm in one eye, 2.5 mm in three eyes, and 3.0 mm in four eyes. In the case series, 11 eyes (68.8%) received PKP with a minimal graft, while five eyes (31.2%) received conventional PKP, including two eyes in which perforation involved the peripheral cornea combined with severe corneal opacity. After surgery, two patients completed a follow-up of half a year, and 14 patients completed a follow-up of at least one year (average, 21.1mo; range, 6–51mo). Figure 1 shows the results for a patient with extensive corneal opacity and vascularisation treated with conventional PKP.

**Symptom Evaluation** Bilateral eye disease was seen in all patients, while discomfort symptoms arose in the perforated eye. In this case series, the most common symptoms were blurred vision (87.5%), redness (81.3%), photophobia (68.8%) and tearing (62.5%), as shown in Table 2. At the final follow-up, most symptoms of discomfort, such as red eye, photophobia and tearing, were improved.

**BKC Activity and Damage Assessment** Although BKC manifested in both eyes of the subjects, the progression typically differed in the two eyes. At the patients' presentation at our hospital, the perforated eyes were classified as BKC with severe activity (A3) and severe damage (D3), while the contralateral eyes were assessed as BKC with no to severe activity (A0-3) and mild to severe damage (D1-3), according to



**Figure 1 Conventional PKP for BKC-combined peripheral corneal perforation with diffuse corneal opacity** A: Corneal perforation at 3 o'clock with severe corneal opacity and neovascularisation; UCVA=2.3 logMAR. B: Contralateral eye indicated corneal infiltration and opacity. C: Eyelid scars and chalazion were found in the perforated eye. D: The patient was associated with rosacea. E: AS-OCT indicating corneal tissue defects and iris prolapse in the perforation area. F: Infrared photo revealing partial meibomian gland dropout. G–H: Corneal inflammation and neovascularisation regressed greatly at 2mo postoperatively. I–J: Photograph at 15mo postoperatively, with UCVA=0.92 logMAR and corneal endothelial cell density=1727/mm<sup>2</sup>. K: Corneal damage to the contralateral eye improved after medication intervention. BKC: Blepharokeratoconjunctivitis; PKP: Penetrating keratoplasty; UCVA: Uncorrected visual acuity; AS-OCT: Anterior segment optical coherence tomography.

Hamada's categorisation<sup>[11]</sup> (Table 3). For BKC management, standard long-term medication with adjuvant therapy such as lid margin cleaning or IPL could directly improve the status of cornea. In the study, the contralateral eyes were treated simultaneously, and detected during the follow-up. At the last follow-up, most perforated eyes were improved to no activity (A0, 81.3%) and presented with no to moderate damage (D0-3). Most contralateral eyes were improved to no activity (A0, 93.8%) and no damage (D0, 68.8%; Table 3).

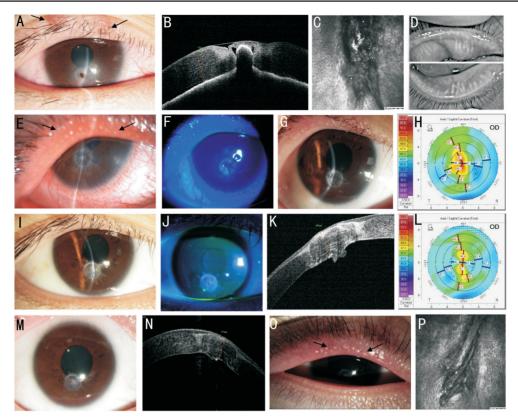
Recovery of Visual Acuity Because visual acuity is a functional measure of activity and damage<sup>[27]</sup>, the recovery of visual acuity was analysed in this study. The mean preand postoperative UCVA values were 1.21 logMAR and 0.56 logMAR, respectively. The results of a paired *t*-test demonstrated that the difference in UCVA before and after surgery was statistically significant (P=0.000, mean±SD: 0.65±0.58, *n*=16, *t*=4.48, 95%CI: 0.34–0.96). Visual acuity improved 3.3 rows on average postoperatively, where UCVA  $\geq 20/40$  (0.52 logMAR) accounted for 31.3%. The mean value of keratometric astigmatism at the final follow-up was 4.48 diopters. PKP with a minimal graft for peripheral corneal perforation showed a satisfactory visual prognosis. A representative case is shown in Figure 2. For corneal perforation involving the pupil zone but not located at the central cornea, PKP with a minimal graft was also practicable, of which representative pictures are shown in Figure 3.

Clinical symptoms	Data
Blurred vision	14 (87.5)
Redness	13 (81.3)
Photophobia	11 (68.8)
Tearing	10 (62.5)
Rubbing	7 (43.8)
White spot	6 (37.5)
Itching	4 (25.0)
Pain	3 (18.8)
Irritation	3 (18.8)
Swelling	2 (12.5)

**Complications** During the mean follow-up period of 21.1mo (range: 6–51mo), none of the patients developed immune rejection or other serious complications. Corneal graft epithelial defects occurred in one eye at two weeks postoperatively, which was attributed to graft protuberance at the graft-host junction. The affected cornea achieved epithelialisation after re-suturing treatment. Complications of steroid-induced elevated IOP and steroid-induced cataracts were not observed during follow-up.

#### DISCUSSION

BKC is one of the most frequent ocular diseases; however, there is currently a lack of standardised treatment for this disease<sup>[28-29]</sup>. BKC complicated by corneal perforation is a



**Figure 2 Minimal-graft PKP for BKC-combined peripheral corneal perforation** A: Perforation was located in the inferior cornea with UCVA=1.0 logMAR. The arrows mark scar formation in the palpebral margin. B: AS-OCT indicating tissue defects in the perforated cornea. C: Laser confocal microscopy showed that *Demodex* was positive in the eyelash follicles. D: Infrared photo revealing severe meibomian gland dropout of the perforated eye. E, F: Corneal status at three days after surgery, with the arrows indicating the meibomian gland obstruction. G, H: Examination at two weeks postoperatively, with curvature of the front cornea =44.8/47.7. I–L: Examination at six months postoperatively; UCVA=0.1 logMAR. AS-OCT displays the profile of the corneal graft, with the curvature of the front cornea =42.3/47.4. M, N: Corneal and palpebral margin status at 39mo postoperatively, with UCVA =0.1 logMAR. O, P: The arrows mark the sign of MGD and blepharitis, with *Demodex* eyelid infestation repositive after discontinuing medication. UCVA: Uncorrected visual acuity; AS-OCT: Anterior segment optical coherence tomography; MGD: Meibomian gland dysfunction; PKP: Penetrating keratoplasty; BKC: Blepharokeratoconjunctivitis.

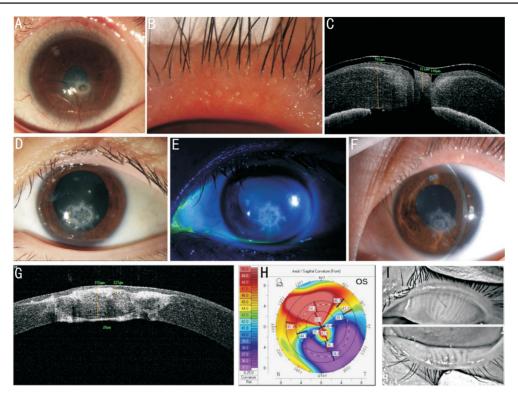
Table 3 Grades	s of the activ	ity and dam	age by BKC
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	Before surgery		Final follow-up	
Patient	Perforated eye	Contralateral eye	Perforated eye	Contralateral eye
1	A3/D3	A1/D1	A0/D0	A0/D0
2	A3/D3	A1/D1	A0/D1	A0/D0
3	A3/D3	A1/D1	A0/D1	A0/D0
4	A3/D3	A0/D1	A0/D2	A0/D0
5	A3/D3	A2/D3	A1/D2	A0/D1
6	A3/D3	A0/D2	A0/D0	A0/D1
7	A3/D3	A0/D1	A0/D3	A0/D0
8	A3/D3	A2/D2	A0/D2	A0/D1
9	A3D3	A0/D1	A1/D1	A0/D0
10	A3/D3	A0/D1	A0/D0	A0/D0
11	A3/D3	A0/D1	A0/D2	A0/D0
12	A3/D3	A0/D3	A0/D0	A0/D1
13	A3/D3	A1/D1	A0/D0	A0/D0
14	A3/D3	A0/D1	A0/D1	A0/D0
15	A3/D3	A3/D3	A2/D2	A2/D3
16	A3/D3	A0/D1	A0/D1	A0/D0

BKC activity A0 (no active inflammation) to A3 (severe inflammation); BKC damage D0 (no damage) to D3 (severe residual damage)<sup>[11]</sup>. BKC: Blepharokeratoconjunctivitis. type of non-infectious perforation that is rarely encountered in clinics. To the best of our knowledge, ophthalmic doctors have limited experience with the disease. This study evaluated the clinical manifestation and management of BKC complicated by corneal perforation and emphasized the importance of early diagnosis and surgery for the disease.

In the study, most subjects were young (mean age: 16.3y), except for one 35-year-old participant. The patients had an average onset of BKC at 13.1y. A delay of 3.2y was noted between symptom onset and presentation at the hospital for corneal perforation. Previous research showed that the mean age of BKC onset was between 3.2 and 4.5y in children, with a second peak in adolescence<sup>[5,11,27]</sup>. In this study, the mean age at the time of diagnosis was older (16.3y), compared with 9.3y in Mexican children<sup>[30]</sup>, 11.1y in another group of Chinese patients, 9.87y in Malay patients, and 8.38y in Indian patients<sup>[23]</sup>.

The diagnosis and treatment of BKC in youths are difficult, especially in children, because they are often unable to communicate their symptoms clearly, and their cooperation is



**Figure 3** Minimal-graft PKP for BKC complicated by corneal perforation involving the pupil zone A: Perforation involved the inferior pupil zone, with neovascularisation extending into the cornea; UCVA=1.7 logMAR. B: Image shows marginal hyperaemia and meibomian gland obstruction. C: AS-OCT indicating tissue defects in the perforated cornea. D–E: Examination at two months postoperatively, with most corneal neovascularisation regressed. F: Examination at six months after surgery, with UCVA=0.92 logMAR. G–H: AS-OCT displays the profile of the corneal graft, with the curvature of the front cornea=39.6/50.4. I: Infrared photo revealing mild meibomian gland dropout of the perforated eye. BKC: Blepharokeratoconjunctivitis; PKP: Penetrating keratoplasty; UCVA: Uncorrected visual acuity; AS-OCT: Anterior segment optical coherence tomography.

limited. In Asia, paediatric BKC seems to have a more severe clinical presentation and a longer delay in diagnosis<sup>[23]</sup>. These factors can partially explain why BKC complicated by corneal perforation occurs mainly in youths with a long history of onset. In this study, BKC complicated by corneal perforation showed severe corneal neovascularisation, with perforation located mainly at the inferior peripheral cornea. Presumably, this location was related to the immunological characteristics of the peripheral cornea, which is predisposed to inflammatory responses. Compared with the central cornea, the peripheral cornea is more sensitive to disorders mediated by antigenantibody complexes because of its proximity to limbal blood and lymphatic vessels<sup>[31]</sup>. The high density of Langerhans cells, combined with the increased concentration of immunoglobulin and complement C1 in the peripheral cornea, promotes immune-driven and inflammatory reactions<sup>[32]</sup>.

BKC is a type of inflammation that involves changes in the eyelids, dysfunction of the meibomian glands and inflammation of the conjunctiva and cornea<sup>[3]</sup>. Multiple factors, including bacterial flora on the lid margin and conjunctiva, unhealthy lipids and abnormal morphology of the palpebral margin, combine on the ocular surface, causing corneal disorders<sup>[33]</sup>. These harmful inflammatory mediators are likely to accumulate in the inferior cornea, resulting in corneal epithelium damage, stroma infiltration, ulcer formation, and ultimately, corneal perforation.

BKC is defined by both subjective symptoms and objective clinical changes. In this study, the participants were assessed for symptoms, as well as activity and degree of damage relating to BKC. Compared with their presentation at our hospital, BKC activity and damage were both reduced at the patients' final follow-up.

In the case series, patients had been treated in local hospitals before coming to our institution, treatments such as wearing lenses or conjunctival flap covering were tried, but with a poor result. In cases of small or self-sealed corneal perforation, bandage lenses or autologous serum can be tired to promote epithelial healing. However, the conservative treatment has potential risks. For instance, although the perforation heals, cornea of the previous perforation area only has a thickness of epithelial layer, rubbing eye or trauma can easily lead to a re-perforation. In addition, many small or self-sealed corneal perforation healed with a shallow anterior chamber and anterior synechia, leading to a poor visual prognosis.

Basen on the above statements, the recommended treatment for corneal perforation is to restore ocular integrity using surgical procedures. Although the most effective therapy is corneal transplantation, the shortage of donor corneas has limited this treatment<sup>[34]</sup>. BKC complicated by corneal perforation has been reported in the literature. Fu and Jones<sup>[35]</sup> mini-descemet stripping endothelial keratoplasty (mini-DSEK) in the management of corneal perforation secondary to BKC in a 14-year-old boy who presented with good visual recovery at the eight-month follow-up. Pant *et al*<sup>[36]</sup> reported keratoplasty using a femtosecond laser lenticule in paediatric patients with corneal perforation secondary to BKC.

The high success rate of PKP in these patients is mainly due to a minimal graft. Compared to PKP or lamellar keratoplasty using a large graft, a minimal graft can reduce the occurrence of immune rejection. In addition, using a minimal graft maximally preserves the recipient corneal endothelium, which simultaneously benefits the healing of the cornea. Besides, when corneal perforation occurs, patients or their guardians will pay more attention to the disease. Thus, patients were follow-up regularly after surgery, and provided with timely medication adjustment and appropriate physical therapy as BKC needs a relentless treatment. To sum up, successful PKP outcomes were attributed to exquisite surgery, proper medication, and specific postoperative care. After surgery, the eyes presented with mild or moderate astigmatism. To obtain better visual acuity prognosis, rigid gas-permeable contact lenses or scleral lenses can be used to correct irregular astigmatism<sup>[37-38]</sup>.

Based on the results of this study, PKP is a safe and effective surgical intervention for vision restoration in patients with BKC complicated by corneal perforation. Early surgical intervention with appropriate treatment is indispensable for preventing serious visual impairment. Although the outcomes of the surgery were favourable in the current study, a randomised study with a larger sample size and longer follow-up times should be conducted in a further investigation. Furthermore, in the current study, the lid margin and conjunctival swabs for bacterial culture were not routinely performed. Future studies should include a greater number of cases and collect lipids secreted from meibomian glands or corneal samples to explore the mechanism of BKC complicated by corneal perforation.

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