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Microbial Keratitis Secondary to Therapeutic Contact Lens Wear

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Abstract

Purpose of Review Therapeutic contact lenses are commonly used to treat various ocular surface conditions that require restoration or maintenance of the corneal epithelium. While this is a very successful treatment modality, it is not without risk. The primary risk associated with bandage contact lens wear is microbial keratitis. This paper will review the literature on the occurrence and outcomes of microbial keratitis in the setting of therapeutic contact lens use, including orthokeratology.

Recent Findings Therapeutic contact lenses are used in various situations including ocular surface disease, post-keratorefractive surgery, and post-corneal crosslinking. Orthokeratology utilizes a rigid contact lens for therapeutic purposes. Though an uncommon occurrence in the setting of therapeutic contact lenses, microbial keratitis can occur and can lead to vision loss even in the setting of prophylactic topical antibiotics.

Summary Despite improvements in contact lens materials that would reduce infection rates, use of modern therapeutic contact lenses can still result in microbial keratitis, even with the use of prophylactic antibiotics. Although incidence rates for microbial keratitis in with therapeutic contact lens use are not available, numerous reports confirm that care must be taken when using therapeutic contact lenses to avoid sight-threatening infections.

Keywords Bandage contact lens · Orthokeratology · Microbial keratitis

Introduction

Therapeutic contact lenses have a wide range of applications with the ability to hasten corneal epithelial healing, stabilize the corneal epithelium, act as a barrier to mechanical eyelid trauma, and protect the cornea from environmental exposure. They provide symptomatic relief and are generally well-tolerated. When used for corneal epithelial defects, the lenses are generally used for up to 2 weeks; after that, other modalities are generally attempted. For other situations, therapeutic contact lenses are sometimes used indefinitely (such as in the setting of a Boston keratoprosthesis). Nevertheless, therapeutic contact lenses, like all extended wear contact lenses, carry an increased risk of adverse events, including sight-threatening microbial keratitis [1–5].

There is ample documented evidence that extended wear lenses pose a greater threat of microbial keratitis compared to daily wear lenses. [1–4] With a higher oxygen permeability, newer silicone hydrogel (SiHy) contact lenses are associated with a reduced adverse event profile compared to conventional hydrogel lenses [2–4] and were approved by the FDA in 2001 for extended wear of up to 30 nights. Premarket studies reported zero cases of microbial keratitis [6–8]; however, contrary to early favorable results, cases of microbial keratitis soon surfaced in post-marketing surveillance studies and smaller case series [9–12]. While the risk of microbial keratitis with extended wear lenses for cosmetic purposes is well-established [2, 10], the risk of microbial keratitis with extended wear lenses used for therapeutic purposes (non-FDA approved) is not as readily recognized. Microbial keratitis occurs in these situations despite the use of high oxygen permeability (Dk) SiHy lenses and despite the use of prophylactic antibiotics, which are prescribed in a majority of cases. Although the risk for infection is low with therapeutic contact lenses, it is not zero.

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We present an overview of microbial keratitis with therapeutic contact lenses used in the treatment of persistent epithelial defects (PED) and other ocular surface diseases (OSD), following laser refractive surgery including photorefractive keratectomy (PRK) and laser in situ keratomileusis (LASIK), and with corneal collagen crosslinking (CXL). Lastly, we address the risk of microbial keratitis in orthokeratology (OTK), which requires extended wear of a therapeutic contact lens in the form of a rigid gas permeable (RGP) contact lens.

Ocular Surface Disease and Persistent Epithelial Defects

Therapeutic contact lenses hasten healing of PED and OSD by reducing the risk of epithelial necrosis and desquamation induced by blink-associated mechanical trauma. They can also decrease patient discomfort and improve visual acuity by creating a more uniform tear film interface otherwise disrupted by corneal irregularities. Bullous keratopathy, neurotrophic keratopathy, limbal stem cell deficiency, dry eye syndrome, band keratopathy, graft versus host disease, ocular rosacea, keratoconjunctivitis sicca, and recurrent corneal erosions are all pathologic states which may warrant placement of a therapeutic contact lens if these conditions are refractory to conventional treatment [6–8, 13–16].

Early reports of microbial keratitis with bandage contact lenses for OSD date back to the 1970s [17, 18]. A more recent 3-year retrospective review by Saini and associates [19••] of 102 cases of bandage contact lens treatment for OSD revealed two episodes of microbial keratitis, resulting in a rate of 2.0%. Both patients had been prescribed lotrafilcon A SiHy lenses and prophylactic topical moxifloxacin 0.5% twice daily, with a range of lens wear from 2 to 272 days and with lens replacement at appropriate intervals. A slightly higher incidence of microbial keratitis (6.7%) was found by Arora and colleagues [9] in a prospective trial of 30 patients fitted with SiHy lenses for PEDs. Cases of microbial keratitis occurred despite the use of topical ciprofloxacin 0.3% or ofloxacin 0.3% four times daily.

In a large review of 23,889 contact lens wearers in Southern India, Sharma and associates [20] identified four cases of microbial keratitis with a therapeutic contact lense prescribed for PED (three) and aphakic bullous keratopathy (one). All cases were secondary to gram-positive bacteria. The overall incidence of microbial keratitis was low at 0.11% (among all CL wearers); however, 14.2% of all microbial keratitis cases occurred in the setting of therapeutic contact lens use. The total number of therapeutic contact lens users within the entire study population and the rate of microbial keratitis among that cohort were not reported. The authors also did not specify whether patients were prescribed prophylactic antibiotics with therapeutic contact lenses before developing microbial keratitis. In this series, there was fortunately no change in BCVA among patients who developed microbial keratitis in a therapeutic contact lens. Smaller case series and individual case reports provide insight into the potentially significant visual morbidity associated with microbial keratitis in therapeutic contact lens use for PEDs and other OSD. A sample of these cases are listed in Table 1 [21, 22].

Park and colleagues [23•] studied the spectrum of bacterial colonization of therapeutic contact lenses prescribed with prophylactic topical tobramycin 3% for recurrent corneal erosion syndrome. After 2 weeks of wear, 22.5% had positive cultures, with *Staphylococcus epidermidis* most commonly detected (7), as well as several cases of Methicillin-sensitive *S. aureus* (MSSA) (5), and Methicillin-resistant *S. aureus* (MRSA) (2), consistent with previous reports of gram-positive organisms most frequently causing microbial keratitis in therapeutic contact lens wear (in contrast to *Pseudomonas aeruginosa* being the most common etiology for cosmetic contact lens-related microbial keratitis). No patients developed microbial keratitis although once positive cultures were identified, they were promptly treated with appropriate topical antibiotics. The investigators hypothesize that the impaired immune mechanisms in the setting of surface disease may be a key risk factor for microbial keratitis once bacteria have gained access to lens surface. [23•] This study highlights the relatively high rate of bacterial colonization in therapeutic contact lens with extended wear for OSD treatment despite the use of prophylactic antibiotics. The rate of infection with therapeutic contact lenses in the setting of immune-mediated diseases such as Stevens-Johnson syndrome and ocular cicatrical pemphigoid could theoretically be even higher given that these patients are more prone to infections at baseline.

Collagen Cross-Linking

Since the early 2000s, collagen cross-linking (CXL) with riboflavin and UV-A light has assumed an important role in the treatment of progressive keratoconus as well as corneal ectasia after LASIK. It is a relatively safe procedure with few adverse side effects. In addition, CXL has been utilized successfully as an effective adjunct in MK treatment by inducing damage to bacterial DNA and RNA leading to bacterial cell death [24]. Reports of using CXL in the treatment of microbial keratitis include gram negative, gram positive, and fungal infections [24, 25]. Nevertheless, its antimicrobial function does not fully protect against new microbial keratitis associated with therapeutic contact lens use after CXL [26••, 27–32].

In a systematic review of the literature, Abbouda and colleagues [26••] identified ten cases of microbial keratitis after CXL. In all cases, either a fluoroquinolone or aminoglycoside antibiotic was prescribed with a therapeutic contact lens after

Table 1 Cases of microbial keratitis in the setting of ocular surface diseases

Authors	Year	Incidence of MK	Lens type	Indication	Antibiotic prophylaxis	Organism cultured	Initial VA; Final BCVA (Snellen)
Kent [18]	1990	NA – 22 cases	NA	a. BK (9) b. Neutrophic keratitis (7) c. Keratitis sicca (3) d. Post surgery (3)	Gentamycin or Tobramycin (12) Other (4)	*Staphylococcus* (2) *Streptococcus* (6) Other GPC (1) Other GNR (4)	NA; 20/40–20/100 (1) 20/200–20/400 (2) CF-HM (13) LP-NLP (2)
Arora [9]	2004	6.7%	Balafilcon A	a. PED b. PED	a. Ofloxacin b. Ciprofloxacin	NA	NA
Koh [21]	2012	NA – 1 case	Lotrafilcon-A	Sjogren's, filamentary keratitis	Levofloxacin	MRSA	20/60; 20/400
Saini [19]	2013	2%	Lotrafilcon-A	a. RES b. LSCD	a. Moxifloxacin b. Moxifloxacin	NA	NA
Todokoro [22]	2015	NA – 1 case	NA	PED	NA	*Corynebacterium propinquum*	20/100; 20/100

OSD, ocular surface disease; *MK*, microbial keratitis; *VA*, visual acuity; *BCVA*, best corrected visual acuity; *NA*, not available; *BK*, bullous keratopathy; *GPC*, gram positive cocci; *GNR*, gram-negative rods; *CF*, count fingers; *HM*, hand motion; *LP*, light perception; *NLP*, no light perception; *PED*, persistent epithelial defect; *MRSA*, *Methicillin resistant Staphylococcus aureus*; *RES*, recurrent erosion syndrome; *LSCD*, limbal stem cell deficiency

CXL prior to the development of microbial keratitis. Half of the cases were secondary to gram-positive bacteria, three were due to gram negative bacteria, two were due to fungus, and one was due to *Acanthamoeba*. A central stromal scar resulted in four cases, and either penetrating or lamellar keratoplasty was required for optimal visual rehabilitation.

Sharma and colleagues [27] highlight therapeutic contact lens mishandling as a major risk factor for microbial keratitis after CXL. The presence of an epithelial defect, hypoxia secondary to the therapeutic contact lens, and concomitant use of topical steroids and/or topical NSAIDs after CXL are additional important risk factors. While CXL without debridement has been attempted as a method for decreasing patient discomforting and obviating the need for a therapeutic contact lens, absorption of riboflavin for successful CXL may not be adequate with this modality. Additional risk factors for microbial keratitis with therapeutic contact lens after CXL include disruption of epithelial integrity from the procedure itself, delayed corneal healing due to patient factors (e.g., diabetes mellitus or atopic disease), and patient mishandling of the therapeutic contact lens. While the former may be unavoidable, proper patient counseling regarding therapeutic contact lens management after CXL cannot be overemphasized.

The precise incidence of MK in the setting of therapeutic contact lens use after CXL has not been reported. However, a sample of cases listed in Table 2, demonstrates the potential severity of microbial keratitis with therapeutic contact lens after CXL. In addition to infections caused by MRSA and MSSA, infections due to *Acanthamoeba*, *Streptococcus salivarius*, and *S. oralis* have been reported. Several of these cases resulted in significant visual morbidity with reduction in BCVA or even in penetrating keratoplasty as a salvage measure for any visual restoration. The consistently young age of patients affected is striking [28–32]. The use of a therapeutic contact lens may shorten healing time after CXL, but this is at the expense of increasing the risk of microbial keratitis.

Post Photorefractive Keratectomy/Laser In Situ Keratomeliusis

Therapeutic contact lenses are used after laser refractive surgery, including both LASIK (in certain situations) and surface ablative treatments such as PRK, to reduce postoperative pain and hasten corneal re-epithelialization. Microbial keratitis following refractive surgery is relatively rare, with an incidence between 0.02 and 0.8% reported for PRK [33, 34] and up to 1.5% with LASIK [35]. Disruption of epithelial integrity in LASIK and PRK may enhance the opportunity for bacterial colonization and invasion. Additional reported risk factors include contact lens manipulation, lack of perioperative antibiotics, and undertreated dry eye syndrome prior to the procedure [34, 36].

While some cases of microbial keratitis with laser refractive surgery occur independent of therapeutic contact lens use, several microbiological studies of therapeutic contact lenses placed after refractive surgery demonstrated moderate rates of bacterial contamination. Liu and associates examined lenses after both PRK and LASEK (laser epithelial keratomilieusis) and found a rate of contamination of 11.7% overall. The most common organism identified was coagulase-negative staphylococcus (CoNS) in six cases, five of which were MRSA [37]. These results are consistent with colonization rates reported by Hondur and colleagues (11.5%) and Haq and associates (16.3%) [38, 39]. Detorakis and colleagues reported slightly higher rates of contaminated lenses among PRK eyes (18.2%) and LASIK eyes (14.8%) [40]. In all studies, no cases of microbial keratitis resulted although topical antibiotic

Table 2 Cases of microbial keratitis in the setting of corneal crosslinking

Authors	Year	Incidence of MK	Lens type	Indication	Antibiotic prophylaxis	Organism cultured	Initial VA; Final BCVA (Snellen)
Rama [29]	2009	NA – case report	NA	Post-CXL	Ofloxacin	*Acanthamoeba*	NA; 20/200, PH 20/40 after PK
Zamora [20]	2009	NA – case report	Balafilcon A	Post-CXL	Ciprofloxacin	*Streptococcus. salivarius, S. oralis, CoNS*	NA; 20/50
Sharma [27]	2010	NA – case report	Balafilcon A	Post-CXL	Moxifloxacin	*Pseudomonas aeruginosa*	NA; 20/200
Rana [31]	2015	NA – case report	Balafilcon A	Post-CXL	NA	*Staphylococcus aureus MRSA*	a. NA; CF b. NA; 20/80

CXL, corneal crosslinking; *MK*, microbial keratitis; *VA*, visual acuity; *BCVA*, best corrected visual acuity; *NA*, not available; *PK*, penetrating keratoplasty; *CoNS*, coagulase negative staphylococcus; *MRSA*, *Methicillin resistant Staphylococcus aureus*; *CF*, count fingers

treatment was initiated immediately at the time of positive detection, perhaps preempting the development of clinically significant microbial keratitis.

A recent retrospective review from three referral cornea and refractive surgery practices identified 13 cases of microbial keratitis with therapeutic contact lens following PRK despite the use of prophylactic antibiotics including tobramycin 0.3% (nine eyes), polymyxin B/trimethoprim (three eyes), and ciprofloxacin 0.3% (one eye) [41]. Four patients had manipulated their lens, and two had replaced the lens without proper cleaning after it fell out. Five cultures were positive for *S. aureus* including a bilateral case of MRSA. In addition, there were cases of *S. epidermidis* (four), *S. pneumoniae* (three), and *S. viridans* (one). Final BCVA ranged from 20/20 (five cases) [to] 20/100 (one case). One eye in the bilateral MRSA case ultimately required penetrating keratoplasty due to impending corneal perforation [41]. Additional examples of microbial keratitis cases after PRK or LASIK are listed in Table 3 [42–45].

Orthokeratology

OTK lenses also require extended wear for therapeutic purposes and therefore, microbial keratitis with OTK is addressed here, as well. OTK was first described in the 1960s, and today utilizes a reverse-geometry rigid gas-permeable contact lens to induce corneal remodeling, specifically flattening, in order to reduce myopic refractive error temporarily. The lenses must be worn overnight for these changes to take place; but even still, a permanent refractive change has not yet been demonstrated. OTK has come into favor as an alternative to refractive

Table 3 Cases of microbial keratitis in the setting of refractive surgery

Authors	Year	Incidence of MK	Lens type	Indication	Antibiotic prophylaxis	Organism cultured	Initial VA; Final BCVA (Snellen)
Kaldawy [42]	2002	NA – case report	NA	Post-PRK	Ofloxacin	*Acanthamoeba*	NA; 20/125 after PK
Donnenfeld [41]	2003	NA – case series	NA	Post-PRK	Tobramycin (9) Polymyxin B/Trimethroprim (3) Ciprofloxacin (1)	*Staphylococcus epidermidis* (4) *S. aureus* (3) *Streptococcus pneumoniae* (3) *MRSA* (2) *S. viridans* (1)	NA; 20/20 (5) NA; 20/25 (3) NA; 20/40 (3) NA; 20/70 (1) NA; 20/100 (1)
Laplace [43]	2004	NA – case report	Filcon V4	Post-LASEK	Ciprofloxacin	S. haemolyticus	20/20; 20/20
Moshirfar [44]	2006	NA – case series	NA	a. Post-PRK b. Post-LASIK	a. Moxifloxacin b. Moxifloxacin	a. *Pseudomonas aeuruginosa* b. *MRSA*	a. 20/20; 20/20 with RGP lens after PK b. NA; 20/60
Wroblewski [33]	2006	0.02%	NA	Post-PRK	Ofloxacin (3) Polymyxin B/Trimethoprim (1) Levofloxacin (1)	*CoNS* (2) *MRSA* (2) Culture negative (1)	20/20; 20/15 (2) 20/20; 20/20 (1) 20/20; 20/30 (1) 20/20; NA (1)

PRK, photorefractive keratectomy; *LASEK,* laser-assisted subepithelial keratectomy; *LASIK*, laser-assisted in situ keratomileusis; *MK*, microbial keratitis; *VA*, visual acuity; *BCVA*, best corrected visual acuity; *MRSA*, *Methicillin resistant Staphylococcus aureus*; *PK*, penetrating keratoplasty; *RGP*, rigid gas permeable

surgery, especially in young patients in whom surgery may be contraindicated and is especially popular in Asian countries where high myopia is prevalent [46–48].

After the first reported case of vision loss secondary to microbial keratitis with OTK in the 1980s, OTK fell out of favor briefly until its reemergence in the early 2000s with the advent of higher Dk lens materials and computer-assisted videokeratography for more accurate fitting of OTK lenses. Safety concerns persisted given the young target population and known infection risk with overnight lens wear. Nevertheless, the FDA approved several OTK lenses in 2002 [46–48].

Throughout the evolution of OTK, there have been continuous reports of microbial keratitis cases. In 2005 alone, there were five reports of severe microbial keratitis with OTK in three different continents. In all five reports, the infections were central, severe, and secondary to aggressive organisms (*Pseudomonas* and *Acanthamoeba* most common), involving multiple brands of lenses, and present in young patients [47]. An extensive review by Van Meter and colleagues demonstrated that well over 100 cases of microbial keratitis with OTK have been reported since 2001 [48].

Since then, Watt and Swarbrick identified 123 published cases of microbial keratitis with OTK between 2001 and 2007. This report expanded upon their initial report in 2005 of fifty cases of microbial keratitis with OTK [49]. Overall, the majority of cases were published in China or Taiwan, and patients were more often young females between the ages of 8 and 15 years old. The majority of microbial keratitis cases occurred within the first year of OTK lens wear, and BCVA after resolution ranged from 20/20 to 20/400 with 29% reduced to 20/200 or worse. They interestingly observed a rise in microbial keratitis cases in 2001 including a large number Acanthamoeba infections (41%) and concomitantly poor visual outcomes with eleven cases (17%) resulting in a BCVA of 20/200 or worse. They hypothesize that a formerly unregulated OTK market in China permitting unapproved contact lens materials, untrained practitioners, and tap water being used as contact solution, were key risk factors associated with this trend [50].

While the *incidence* of microbial keratitis in OTK has declined in Asian countries, it remains a worldwide issue. For example, nine cases of microbial keratitis were reported between 1997 and 2005 in Australia in a study by Watt and colleagues. This representative sample, identified via a retrospective survey, shared many characteristics with the Asian cohort previously described. The majority of patients were young females, overnight wear was the most common prescribing method, and *Pseudomonas* sp. or Acanthamoeba were the most frequently identified pathogens. Improper lens hygiene was the most prevalent risk factor. Fortunately, there was no loss of BCVA in 78% of cases [51].

The most recently reported overall rate of microbial keratitis with OTK is estimated to be approximately 7.7 per 10,000 patient years (0.077%), although it may be higher due to underreporting [52•]. This number is small but significant given the young target population, frequency of highly virulent pathogens, and potential for severe morbidity. While the permanence of reduction in myopia progression with OTK has yet to be proven in prospective studies, the long-lasting damage to vision from microbial keratitis with OTK is evidenced in published case reports and case series [53, 54].

Discussion/Conclusions

One of the earliest published reviews of microbial keratitis with therapeutic contact lenses identified six cases of microbial keratitis out of 110 lens users (5.5%) [17]. Since that time, practice patterns have improved with the advent of higher Dk SiHy contact lens materials and the routine use of prophylactic antibiotics with therapeutic contact lenses. Although the overall rate of microbial keratitis with therapeutic contact lenses for all indications has not been determined, there is indeed evidence in the literature of lower microbial keratitis rates with SiHy lenses of approximately 18/10,000 [2] compared to conventional hydrogel lenses at approximately 29/10,000 [10]. However, as we have demonstrated, cases of microbial keratitis with therapeutic contact lens still occur.

Extended wear is fundamental to the therapeutic effect of therapeutic contact lenses, and as such, this fundamental risk factor for microbial keratitis cannot be eliminated. However, additional contributors may be modifiable, including appropriate antibiotic choice and adequate dosing regimen, scheduled lens replacement, regular follow-up, and judicious patient selection for bandage contact lens placement. In addition, counseling patients on reasons to seek immediate evaluation, proper lens hygiene and warning signs of infection must be emphasized.

Therapeutic contact lenses are undoubtedly a useful therapeutic option; however, we should be acutely aware of the risk of microbial keratitis when prescribing them to our patients. As is evidenced in this review, the advent of modern high Dk lens materials and the use of prophylactic antibiotics can provide a false sense of security to providers and wearers of therapeutic contact lenses. Similarly, OTK carries a risk of microbial keratitis with potentially significant consequences that should not be overlooked, especially given the elective nature of this treatment. With any therapeutic contact lens use, some patients who develop microbial keratitis will be fortunate enough to recover full vision; others could suffer significant and irreversible visual morbidity.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

None of the authors have any financial interests in any of the techniques or products discussed in this manuscript.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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