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Review Article

Microbial Keratitis in Contact Lens Wearers

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Abstract

Contact lens (CL) wear is a common predisposing factor of microbial keratitis (MK). MK in CL wearers is a potentially sight-threatening corneal infection. The causative organism in all MK varies by geographical location and predisposition factors. The most commonly recovered causative organism in CL related MK is bacteria followed by fungi and *Acanthamoeba*. This review focuses on the incidence and causative organisms of MK in CL wearers. Awareness of contributory risk factors for MK in CL wearers is important to follow safer lens wear modalities and hygiene regimes to avoid possible infection. In developed nations, most MK in contact lens wear is by bacterial origin, whereas fungus is the leading causative agent in developing countries. The most common pathogens implicated in bacterial keratitis are *Staphylococci* and *Pseudomonas*. Some of the fungi that commonly cause fungal keratitis include *Fusarium*, *Aspergillus* and *Candida* species. *Acanthamoeba* keratitis is also a growing clinical problem both in developed and developing countries.

INTRODUCTION AND EPIDEMIOLOGY

Microbial keratitis (MK) is an inflammation of the cornea with sight-threatening potential. It can lead to serious visual impairments followed by permanent visual loss if untreated. The predisposition factors for the MK include ocular surface disease, ocular trauma, ocular surgery, contact lens (CL) wear and systemic diseases. CL wear is one of the most significant predisposition factor for CL related MK [1-5]. A number of CL complications such as mechanical, hypoxic, immunologic and hypersensitivity reactions mimic infectious keratitis. The prevalence of MK has increased ever since the 1970s when soft CLs were introduced and is gradually increasing over time. About 43% of the corneal ulcers are mainly due to soft CL wear [6]. CL related MK is caused by bacteria, fungi, parasites and viruses. Among the microbes causing the MK, fungal keratitis accounts for about 50% of all cases of culture-proven MK in some developing countries. Fungal outbreak caused by *Fusarium* in CL wearers in 2005 -2006 and the *Acanthamoeba* outbreak in 2007 have alerted the eye care community and public to focus their attention on the CL related MK. Globally about 140 million people wear CLs for correcting refractive errors. About 3.5 million people have begun to wear CL every year but 2-3 million people discontinue CL wear at about the same time [7]. About 41 million people wear CLs in

the United States (US) [8]. Among them, two-thirds of (67%) all CL wearers are females. The average age of CL wearers is in low 30s. However, age varies from 18 or under (10%), 18-24 (15%) and 25-44 years old (50%). In other countries such as Nepal, the average age of CL wear is 24 years and older than 36 years in United Kingdom (UK). Age associated CL related infectious keratitis has also been reported. The CL associated keratitis is more significant in younger patients than the elderly. However the severity of the infection is more in elderly than the younger patients and the elderly patients have multiple and more diverse risk factors, making prevention difficult [9]. Most people wear CL to correct nearsightedness. The percentage of different kinds CL usage also varies among CL wears. Among them, daily wear soft CLs (80%), 1 to 2-week disposable CLs (50%) and extended wear soft CLs (15%). More than 80 % of CL wearers go to an optometrist for their eye care [10]. Among all lenses fitted, soft CLs continue to account for about 90%. The risk of MK among CL wearers is about 80-fold greater than among healthy non wearers [11]. Soft CL wearers were found to be frequently susceptible to MK [12-14]. Comparatively soft CLs, especially extended-wear CLs, are significantly associated with MK than the daily wear soft CL and hard CL wearers [12,15-19]. The high incidences of MK in extended wear soft CL and hard CL wearer has led to the decreased usage of these lenses in many countries. This has further prompted patients to prefer daily wear lenses [20]. In Austria, patients are instructed by ophthalmologists not to wear any CLs on an extended wear basis. Ophthalmologists recommend the use of disposable CLs for daily wear only [20]. The relative risk of MK for extended wear soft CL wearers was 36.8 times more than that of rigid gas permeable CL wearers [21]. Disposable CLs with a daily wear schedule could also become a pre disposing factor for MK [20]. Cosmetic CL wear is also associated with MK. It was recently reported that the cosmetic usage affects the surface properties of the CLs. This study showed that there is an increase in contact angle and pixel brightness when the CLs were coated with cosmetics such as common hand creams, eye makeup removers, and mascaras [22]. The pigments on the surface of the cosmetic CLs allow the bacteria to adhere on their surface [23]. Nearly one million cases of CL complications occur annually in the United States [24]. The annual incidence of MK is estimated to be 4-21 per 10,000 CL wearers.

Risk factors for contact lens related MK

The leading risk factor for MK is CL wear. The incidence of MK was significantly increased from 40% to 52% during 2008-2012 [1]. The incidence of MK ranged from 0.4 to 5.2 per 10,000 person per year for rigid gas-permeable and more than 20 per 10,000 person per year for soft CL wearers [25]. The common risk factors for CL related MK is poor storage case hygiene, infrequent storage case replacement, and overnight CL wear [26,27]. In addition, the major risk factors for CL associated MK are overnight use of daily wear lenses, using lenses on extended wear schedule for longer duration, being of male gender, inadequate hygiene of the CLs, and poor CL storage case cleaning [28,29], use of tap water for storing lenses, failure to air-dry lens-storage cases or use of one-step hydrogen peroxide disinfectant [30-33]. About quarter of the cases of MK are due to the contaminating organisms in the CL case and solution [34]. Microbial contamination of CL storage case was a great risk for gram-negative bacterial infection among soft CL-wearers [35]. Compared to bacterial or fungal keratitis, patients with *Acanthamoeba* keratitis are more likely to be in younger patients and to have a ring infiltrate or disease confined to the epithelium [36]. According to a national survey conducted in US, the unsafe eye care practices lead to severe eye infection and more than 99 % of people follow at least one unsafe practice during CL usage. The majority of wearers reported three unsafe practices, 1) keeping their CL cases for longer than recommended (82%), 2) topping off solution in the case (55%) or 3) wearing their lenses while sleeping (50%) [37]. Complications associated with CL wear ranges from milder to severe conditions. CL wear can cause a change in corneal physiology, which can lead to epithelial, stromal, and endothelial compromise. Apart from MK, the other complications associated with CL wear include lens deposition, allergic conjunctivitis, giant papillary conjunctivitis, peripheral infiltrates and neovascularization. To avoid complications, it is necessary to discontinue CLs, changes in CL wearing schedules, materials, care solutions and topical therapy [38,39].

Microbial keratitis and causative organism associated with contact lens

Various microorganisms are associated with MK in CL wearers. The clinical manifestation of MK can be related to the broad type of causative organisms. The MK in CL wearers varies by predisposing factors and climatic conditions. The most common bacterial pathogens associated with MK implicated are *Staphylococcus* and *Pseudomonas* species. They are more frequent in temperate climate regions. Whereas fungal keratitis is more frequent in tropical or sub-tropical climates. *Fusaria* are the most common fungal pathogen associated with CL related fungal keratitis. While *Acanthamoeba* keratitis seems to be a growing clinical problem in CL wearers, viral keratitis is poor understood.

Bacterial Keratitis

Bacterial keratitis is a potentially sight-threatening corneal infection in CL wearers [40]. Approximately 90% of MK in CL wearers is associated with bacterial infection [41]. The bacteriological profile in keratitis shows huge disparities amongst populations living in both western and in developing countries. The incidence varies considerably between these countries due to the fact that less industrialized countries have significantly lower number of CL wearers, hence fewer CL related infections. For example, US have an incidence of 11 per 100,000 persons for MK as compared to 799 per 100,000 persons in Nepal. Bacterial keratitis in CL wearers is mostly associated with gram-negative bacteria such as *Pseudomonas, Serratia, Acinetobacter, Klebsiella spp* and other bacterial species. Most of the bacterial species listed (Table 1) were isolated and identified from CL, CL storage case, CL solution and corneal scraping of CL wearers. The CL associated keratitis is also caused by gram-positive bacteria such as *Staphylococcus, Streptococcus spp.* and others [42]. Ormerod *et al*. reported that staphylococcal species, *P. aeruginosa* and *S. pneumoniae* as major isolates in MK in North America [43], whereas in Sweden, *S. aureus* and *S. epidermidis* were the most common gram-positive bacteria in central microbial keratitis while *P. aeruginosa* was the most common gram-negative bacteria [44]. MK caused by gram-negative bacteria is more severe and associated with a worse visual prognosis than that

Table 1: List of bacteria isolated from CL related bacterial keratitis.

Pathogen	Source	References
Gram negative bacteria		
Pseudomonas aeruginosa and other *Pseudomonas spp.*	CL , CL storage case, CL storage solutions, corneal scrapings and orthokeratology	[1-3, 13, 17, 19, 28, 30, 35, 45, 47, 49-80]
Serratia marcescens, Serratia liquifaciens and other *Serratia spp.*	CL, CL storage cases, corneal scrapings	[3, 19, 49, 53, 56, 57, 63, 64, 75, 81]
Acinetobacter calcoaceticus, Acinetobacter baumanni and other *Acinetobacter spp.*	CL, CL storage cases and corneal scrapings	[56, 57, 73, 79, 82-84]
Klebsiella oxytoca and other *Klebsiella spp.*	CL, CL storage cases and corneal scrapings	[3,13,56,57,67,75]
Haemophilus influenza	CL and corneal scrapings	[19,75,85]
Achromobacter xylosoxidans	CL, CL storage cases, and CL storage solution	[73,86-88]
Eneterobacter gergoviae and other *Enterobacter spp.*	CL and CL storage cases	[57,66,76,89]
Aeromonas hydrophila and other *Aeromonas spp.*	CL, CL storage cases, CL wear	[75,82]
Moraxella lacunata and other *Moraxella spp.*	CL	[3,19]
Stenotrophomonas maltophila	CL, CL wear	[67,75,82]
Citrabacter freundii and other *Citrobacter spp*.	CL, CL storage cases and corneal scrapings	[56,85,89]
Alcaligenes xyloxidans and other *Alcaligenes spp.*	CL and CL storage cases	[19,56]
Morganella morganii	CL	[19]
Xanthomonas spp.	CL storage cases	[56]
Proteus mirabilis	CL and CL storage cases	[62]
Comamonas acidovorans	CL wear	[90]
Herellea vaginocola	CL storage case and Corneal scrapings	[91]
Gram Positive bacteria		
Staphylococcus aureus, Staphylococcus epidermidis and other *Staphylococcus spp.*	CL, CL storage case, corneal scrapings, and CL care solution	[1,3,19,40,53,54,60,62,63,65,66,68,69,76-78,82 84,85,89,91-96]
Streptococcus pneumonia, Streptococcus viridians, α-hemolytic Streptococcus and other *Streptococcus spp.*	CL, CL storage case, CL storage solutions and corneal scrapings	[3,19,52,63,68,73,77,84,85,96]
Bacillus cereus	CL, CL storage case and CL storage solutions	[40,97]
Micrococcus spp.	corneal scrapings	[73,85,96]
Diphtheroids	CL, CL storage case	[3,56]
Propioni bacterium acnes	CL, CL storage case	[76,77,98]
Cornybacterium propinquum and other Corynebacterium spp.	CL and CL wear	[19,96,99]
Clostridium	Corneal scrapings	[85]
Micrococcus	CL storage case	[56]
Enterococci	CL storage solution and corneal scrapings	[92]
Peptostreptococcus spp., Aerococcus viridians, Nocardia spp.	CL wear	[96]

of the most other common bacterial pathogens. However, *Pseudomonas* and *staphylococci* are the most common bacterial pathogens implicated in CL associated bacterial keratitis. *P. aeruginosa* accounts for 37-60% of CL related corneal bacterial infection [45]. Extended wear soft CL wearers are mostly associated with the increased incidence of *P. aeruginosa* infection [17,46]. The alkaline protease and gelatinase are produced by the *P. aeruginosa* during pseudomonas keratitis. These two enzymes play an important role in the invasion of corneal epithelium and pathogenesis of CL associated Pseudomonas keratitis [47]. The strong association between *P. aeruginosa* and CL related infection is intriguing. The lens, storage case, and ocular environment may offer a suitable survival niche for this environmental organism. *P. aeruginosa* can adhere and colonize lens materials during use and survive in CL storage cases, partly through its ability to grow as a resistant biofilm on lenses and cases, and partly due to innate or acquired resistance to CL disinfectants [48].

Factors which influence the etiology and pathogenesis of bacterial keratitis vary. They include, wear of CLs, ocular surface diseases, corneal trauma, use of immunosuppressive medications and post ocular surgery especially corneal graft. CL related corneal ulcers in the general population have increased from almost 0% in the 1960s to 52% in the 1990s. Epidemiological studies have shown that CL wear is the significant risk factor for bacterial corneal infections. Extended wear soft CL wearers have a higher annual incidence of ulcerative keratitis than the daily wear soft CLs. The same study provided an interesting revelation that smokers are three times more prone to develop keratitis than non-smokers. The rate of ulcerative keratitis in smokers are 1 in 2,500 daily wear CL wearers as compared to 1 in 500 in extended wear CL wearers per year [100].

Risk factor and symptoms of bacterial keratitis

The major risk factor for the bacterial keratitis is sleeping with CLs among CL wearers [101]. Patients with diabetes mellitus, dementia or chronic alcoholism appeared to be at higher risk

and trauma was rarely a factor [52]. Bacterial keratitis occurred most frequently in spring and least frequently in winter. Patients who live in suburban areas are mostly affected by CL associated bacterial keratitis [102]. Bacterial biofilm formation on CLs and CL storage cases may be a risk factor for CL associated bacterial keratitis. Bacterial biofilm was present more frequently on CL storage case surfaces compared with CL surfaces [53]. The avascular corneal stroma is particularly susceptible to bacterial infection [19]. The predominant clinical features reported in bacterial keratitis were eye pain and redness with a decrease in visual acuity and stromal infiltration [103,104].

Diagnosis and treatment of bacterial keratitis

Identifying the causative organism is very important for the proper treatment of the MK [84]. Microscopic observation of corneal scraping using stained smears is useful for diagnosis of bacterial keratitis. Different stains such as gram stain, giemsa stain, and Ziehl-Neelsen stain are widely used to identify bacteria in keratitis. White-light confocal microscopy is used for the diagnosis of bacterial keratitis [105]. Culturing of the corneal scrapings is also useful for diagnosing bacterial keratitis. The samples are directly inoculated onto different culture media such as sheep blood agar, chocolate agar, thioglycollate broth, Robertson cooked meat medium, Lowenstein Jensen medium, and middle brook medium for the detection of bacterial growth [28,106]. Immunological techniques such as direct immunofluorescence, immunoelectrophoresis, immunohistochemistry, enzyme immunoassays, agglutination, radioimmunoassay and other molecular techniques are also useful for the detection of bacterial antigens in patients with bacterial keratitis [107].

Bacteria isolated from bacterial keratitis must be periodically tested against available antibiotics in order to determine the current resistance pattern [108]. The disc susceptibility method provides quantitative measurements that are critical for epidemiology and drug resistance surveillance. The resistance to antibiotics was evaluated with the standard disc diffusion method. The resistance rate and the penetration of the antibiotic at the level of infection must be considered when choosing a therapeutic agent in bacterial keratitis [19]. Topical application of combination of antibiotics such as cefazolin and gentamicin has been considered as the gold standard for the therapy of bacterial keratitis [109]. The gram-negative bacteria associated bacterial keratitis cases should be immediately treated with quinolones and erythromycin whereas the gram-positive associated keratitis should be treated with a combination of aminoglycosides and erythromycin [77]. Fluoroquinolones and aminoglycosides were used in the treatment of *P. aeruginosae* keratitis [47,110]. Fluoroquinolones were shown to be effective against both gram-positive and gram-negative bacteria [19]. Chloramphenicol and cefazolin are very effective against gram-positive bacteria [19]. Aminoglycosides (tobramycin, neomycin, and gentamicin) also provide a broad spectrum of activity against gram-negative pathogens [19]. Ofloxacin, or a combination of gentamicin and cephazolin, are excellent first-choice therapies, as little resistance has developed to these antibiotics [2]. Other antibiotics such as gentamicin, tobramycin, ciprofloxacin, clindamycin and vancomycin are used for the treatment of bacillus keratitis [110], whereas cephalosporin or vancomycin were used for the initial treatment of *staphylococcus* keratitis [111]. A recent study has shown that novel ciprofloxacin-releasing silicone hydrogel CLs may be a future treatment modality for bacterial keratitis, especially for *Pseudomonas* keratitis [112].

Fungal keratitis

Fungal keratitis is a major cause of corneal blindness in developing countries. 5 to 20% of all infectious keratitis cases are of fungal etiology [54,55]. Possible risk factors of fungal keratitis are ocular injury, long-term therapy with topical or systemic steroids, immunosuppressive agents, and underlying diseases such as pre-existing corneal surface abnormality and wearing CLs [113]. Fungal keratitis is the frequent cause of MK in India and the incidence ranges from 35 to 50%. The reason for high incidence is due to the tropical climate and a large agrarian population. *Aspergillus* and *Fusarium* species are frequently isolated as causative agents of CL related MK in India [114]. In developed countries, such as the UK and USA, bacteria cause the majority of corneal infections in CL wearers. However, fungal keratitis also exists in lesser percentage. A recent study on Danish population living in temperate climate revealed that trauma including CL wear was associated with filamentous fungal keratitis and with a poor visual outcome [115]. The CL associated fungal keratitis is also observed in immunosuppressive diseases such as HIV [116] and diabetes [117]. The fungal species listed in the Table 2 were isolated from CL, CL storage case, CL solution and corneal scraping of CL wearers. Fungal genera such as *Fusarium, Aspergillus*, *Candida* and other species are associated with fungal keratitis [118-121]. However, *Apsergillus* species are the most common cause of fungal keratitis in CL wearers and it is prevalent in moist, subtropical and tropical climates worldwide. Fungal keratitis carries worse prognosis than any other types of MK. The disease is more likely to affect the eye than the bacterial keratitis [122]. The diagnosis of fungal keratitis is delayed and more over the fungi are more resistant to treatment that makes the fungal keratitis to cause more sight threatening effects than other MK types.

Fusarium Keratitis Outbreak in Contact lens wearers

From January 2005 to May 2006, 33 cases of CL related *Fusarium* keratitis was identified in Hong Kong. Most of the patients were young adults and showed symptoms such as occular pain, redness, photophobia and tearing. Using B and LReNu CL solution was strongly associated with *Fusarium* keratitis among CL wearers in Hong Kong [133]. Another outbreak of *Fusarium* keratitis in CL wearers in the northeastern United States was observed in 2006. 15 cases of *Fusarium* keratitis were reported in CL wearers between July 2005 and May 2006 (16.4 cases/yr). All 15 patients used ReNu brand CL solution when they developed keratitis [134]. In Singapore, during March 2005 to May 2006, 66 patients were diagnosed with *Fusarium* keratitis associated with CL wear; the estimated annual national incidence is 2.35 cases per 10,000 CL wearers. The majority (62 patients (93%)) CL wearers were reported using ReNu brand CL solution [135]. Therefore B and LReNu with MoistureLoc1 were permanently withdrawn from the market globally in May 2006 [124]. *F. solani* was recovered from an opened bottle of Moisture Loc solution provided by a patient with CL associated *Fusarium* keratitis in New York State [33].

Table 2: List of fungi isolated from CL related fungal keratitis.

Pathogen	Source	References
Fusarium solani, Fusarium oxysporium and other *Fusarium spp.*	CL, poor CL hygiene, CL solution, CL storage cases and corneal scrapings	[13,14,30,31,33,54-56,61,64,85,123-127]
Candida albicans	CL, CL storage cases, and corneal scrapings	[56,73,78,85,95,127,128]
Aspergillus flavus, Aspergillus versicolor and other *Aspergillus spp.*	CL and CL storage cases	[34,56,78,129]
Alternaria alternate	CL wear	[119,120,130]
Cephalosporiumacremonium and other *Cephalosporium spp.*	CL and CL storage cases	[56,127,131]
Rhodotorula, Cryptococcus, Candida and *Wangiella dermatidis*	CL soaking solutions	[40]
Cryptococcus laurentii	CL	[117]
Purpureocillium lilacinum and other *Paecilomyces*	CL	[127,132]
Exophiala spp, Phoma spp.	CL storage cases	[56]

Risk factors and symptoms of fungal keratitis

The occurrence of fungal keratitis has been associated with many risk factors such as ocular trauma, diabetes, surgery and use of topical corticosteroids, CL wear and antibiotics [118]. One of the most important risk factors for infectious keratitis is CL wear [136]. People wearing any CL can get fungal keratitis. The practices such as improper disinfection of CL, using contaminated lenses, contaminated CL containers, contaminated cleaning solutions, wearing CLs during eye infections and contamination of CLs through the introduction of microorganisms from the environment also lead to disease development. The principal risk factors for *Candida* infection were reported to be trauma or cosmetic CL wear, with ocular surface disease or a prior penetrating keratoplasty [128]. Pathologies of fungal keratitis related to CL wearing occur in the anterior segment of the eyeball and can be seen as serious inflammation. The most significant clinical features of CL associated *Fusarium* keratitis include central lesions, paraxial lesions, and the peripheral lesions in the eye [31]. Patients with *Candida* infections were reported to have a severe visual outcome [115].

Diagnosis and treatment of fungal keratitis

Fungal biofilm formation can be studied using a simple microscopic investigation of corneal scraping stained with 10% potassium hydroxide in the laboratory. For the detection of fungal growth, the corneal scrapings are directly inoculated onto Sabouraud dextrose agar, potato dextrose agar and brain heart infusion broth and incubated at 25°C [28,106]. The fungal biofilms can be quantified using metabolic activity assay and dry weight measurements. Confocal scanning laser microscopy, scanning electron microscopy, fluorescence microscopy and antifungal susceptibility assays are widely used to identify, quantify and evaluate the fungal morphology *in vitro* [137,138]. Early diagnosis and immediate treatment is important to prevent loss of vision and blindness for the patient with fungal keratitis. It usually requires a prolonged course of treatment with the antifungal agents. Fungal keratitis was often treated with a combination of topical and systemic antifungal medications. 1% voriconazole and topical amphotericin B solution has been shown to be highly effective for *Alternaria* keratitis [119-121,130]. Antibiotics such as cephalosporins, aminoglycosides, natamycin and amphotericin B are effective against *Fusarium* keratitis [30,123]. Whereas econazole, amphotericine, itraconazole and voriconazole are used for the treatment of *Candida* infections [128].

Amoebic keratitis

Acanthamoeba keratitis was first reported by Jones et al in 1973 [139]. *Acanthamoebae* are free living protozoa found in air, soil, fresh water, salt water, drinking water, chlorinated swimming pools, and hot tubs [140,141]. The *Acanthamoeba* species such as *A. castellanii* and *A. polyphaga* are mostly associated with CL related keratitis [14,30,53,61,84,85,130,139,142-153]. The other protozoa involved in *Acanthamoeba* keratitis include *Naegleria spp, Vahlkampfia spp* and *Hartmannella spp.* [56,57,154]. *Acanthamoeba* keratitis primarily occurs among soft CL wearers [155,156]. The *Acanthamoeba* cysts are resistant to extreme temperature, desiccation and disinfection. Therefore, these protozoa are ubiquitously present in the environment [157]. Some *Acanthamoeba* keratitis are painful and cause progressive infection of the cornea that can result in loss of vision whereas others are reported to be painless [92]. *Acanthamoeba* can directly infect the cornea, usually after trauma, associated with contaminated water or soft CL wear [158]. The initial feature of *Acanthamoeba* keratitis includes decreased corneal sensation. Which in turn has contributed to the misdiagnosis of *Acanthamoeba* as herpes simplex keratitis. Therefore, physicians should consider *Acanthamoeba* keratitis as an alternative diagnosis in patients with presumed herpes simplex keratitis with decreased corneal sensation [159]. Complications of *Acanthamoeba* keratitis include dacryoadenitis, corneal melting and scarring, severe secondary glaucoma, cataract, and chronic anterior segment inflammation [160]. Progression of the disease led to a cloudy cornea with a stromal ring infiltrate, poor vision, elevated intraocular pressure, mature cataract and finally corneal melt [161]. *Acanthamoeba* keratitis can develop as co-infections in patients' eyes with advanced bacterial keratitis [58]. Co-infection of *Acanthamoeba* keratitis with *P.aeruginosa* was reported recently [59]. However, the exact clinical characteristics of such mixed infections remain unknown. The incidence of *Acanthamoeba* keratitis is about 1% among culture-positive

infective keratitis in India [162]. In Europe and the United States, the incidence among CL wearers is 1.65 to 2.01 per million CL wearers per year by epidemiologic estimation [163,164].

National outbreak of Acanthamoeba Keratitis

The first outbreak of CL associated *Acanthamoeba* keratitis was reported from US in 2007 [150]. The annual incidence of *Acanthamoeba* keratitis in US is 1-2 cases per million CL wearers [163]. A national survey conducted in January 2007 by center for disease control and prevention (CDC) revealed an increasing number of *Acanthamoeba* keratitis cases during 2004-2006 compared to 1999-2003. The national outbreak investigation was initiated on March 16, 2007 to study the *Acanthamoeba* keratitis. Of the 221 patients identified from 37 states, 71% of them had infections and 88% of them were soft CL wearers. The most frequently reported symptoms of these patients include pain, redness, and sensitivity to light and sensation to foreign bodies. This investigation of a national *Acanthamoeba* keratitis outbreak identified that use of Advanced Medical Optics Complete Moisture Plus (AMOCMP) CL solution as the primary risk factor for infection. AMOCMP is a multipurpose CL solution used for disinfecting, rinsing, cleaning, and storing lenses. This study highlights the importance of promoting safe hygienic practices among new wearers of CLs, as well as the need for standardized anti-*Acanthamoeba* testing of CL solutions.

Risk factors and symptoms of Acanthamoeba keratitis

The major risk factors for *Acanthamoeba* keratitis are CL storage cases and poor hygiene practices such as usage of homemade saline rinsing solutions and rinsing of lenses with tap water [57,145,147,164]. Other risk factors include CL solution reuse/topping off, rub to clean lenses, shower wearing lenses, lens replaced (quarterly), age of case at replacement (<3 months), extended wear and lens material type [48]. The clinical symptoms and signs of the disease include itching, redness, pain, burning sensation, ring infiltrates in the cornea, multiple pseudodendritic lesions on the cornea with stromal infiltrate and loss of vision [129,144-146]. The patient with painless *Acanthamoeba* keratitis complained of photophobia but not of ocular pain. The affected eye showed corneal edema, central stromal thickening, descemet's striae as well as fibrin deposits on the corneal endothelium and in the anterior chamber [92]. The other signs of CL associated *Acanthamoeba* are severe ciliary injection, satellite lesions, and radial keratoneuritis [165].

Diagnosis and treatment of Acanthamoeba keratitis

The corneal scrapings and CL solutions can be examined for cysts and trophozoites by using a standard light microscope at higher magnifications. All the corneal scrapings and CL solutions were inoculated onto plates containing 2% non-nutrient agar overlaid with heat-killed *Escherichia coli* and incubated at 27 °C. After 3–4 days, the plates were monitored with an inverted microscope for the outgrowth of *Acanthamoeba* [166]. Methods such as confocal microscopy, PCR, real-time PCR and DNA sequencing are used for early diagnosis and treatment of *Acanthamoeba* keratitis [149,166]. Combination chemotherapy has been shown to be more effective than monotherapy. Topical neomycin-polymyxin B and metronidazole eye drops, moxifloxacin hydrochloride drops, vancomycin drops, amphotericin B drops, amikacin drops, propamidineisethionate ointment, oral ketoconazole, prednisolone and other antibiotics such as clotrimazole, polyhexamethylenebiguanide, and chlorhexidine were found to be effective in treating the *Acanthamoeba* keratitis [130,142,144,147,159,167]. Benzalkonium chloride preserved saline and solutions containing thimerosal with edentate resulted in killing the *Acanthamoeba* [168].

Viral keratitis

Viral keratitis was also observed in CL wearers, especially in daily wear CLs. Nilsson and Lindh have reported that 38% viral keratitis was observed in patients suffering from eye diseases [169]. Soft CLs were shown to be contaminated by hepatitis B virus [170]. Currently approved methods of chemical and thermal lens disinfection methods are reported to be efficient means to inactivate HSV [171]. *Acanthamoeba* keratitis may be present as a secondary or opportunistic infection in patients with herpetic keratitis [151]. The finding of HTLV-III in tears, the conjunctiva, and the cornea indicates the remote possibility that acquired immunodeficiency syndrome (AIDS) can be spread by instruments in contact with the eye, specifically trial CL. Recent studies reveal that heat disinfection may not be adequate, thereby, leaving only hydrogen peroxide systems as a potentially effective method of inactivating large titers of the virus [172]. The presence of human immunodeficiency virus (HIV) particles in the tear fluid, on the conjunctival surface or in the CLs of patients with chronic HIV infection has made it necessary to establish better guidelines for decontamination of instruments during ophthalmological procedures. Tervo *et al* developed disinfection procedures in the Helsinki University Eye Hospital to prevent of HIV transmission during ophthalmological procedures [173]. Vogt *et al* have tested the ability of commercially available CL solutions to disinfect CLs exposed to HTLV-III and found to be effective [174]. Rohrer *et al* reported all viral contaminants were completely inactivated after four minutes of microwave exposure of hydrophilic CLs [175]. The recurrence rates of herpes simplex viral keratitis in CL wearer are higher compared to non-CL wearers [176]. Herpes simplex keratitis reactivation was occurred in patients with the use of rigid gas permeable CLs [177].

Risk factors and Symptoms of viral keratitis

The most significant risk factor for HSV keratitis is a past history of ocular HSV [176]. The recurrence rate for HSV may be higher in the second year than in the first year [178]. The clinical presentations of patients with CL associated herpes simplex keratitis include pain, redness, gradual decrease in vision and parcentral large stromal infiltrate with a central perforation [179].

Diagnosis and treatment of viral keratitis

Herpes simplex keratitis (HSK) is an ocular infection that threatens eye sight considerably. A rapid laboratory diagnosis is very essential to treat HSK keratitis. Conventional virology techniques are often expensive and time consuming. Corneal impression cytology is an inexpensive and very simple technique in which corneal smears were obtained by pressing the surface of one end of the sterile glass slide gently on the corneal lesion. Smears

were stained by an immunoperoxidase or immunofluorescence assay for the detection of HSV-1 antigen using a polyclonal antibody to HSV-1 [180]. HSV keratitis can also be diagnosed by using shell vial assay which employs the cell lines of corneal origin such as human corneal epithelial cell line (HCE) and the Vero cell line that have been shown to be excellent substrates for the growth of HSV-1 and HSK isolated from the cornea [181]. A simple investigation like giemsa stain, immunoperoxidase assay and PCR may offer a clue to the diagnosis [179].

Oral acyclovir therapy may be effective in preventing the herpetic infection [179,182]. Continuous application of human leukocyte interferon with CLs is effective in the treatment of herpetic keratitis [183]. Kasparov *et al* demonstrated the efficacy of microdiathermo coagulation (MDC) in the treatment of herpetic keratitis [184]. Antiviral agents such as trifluridine, acyclovir, idoxuridine and vidarabine were more effective. Other topical antiviral agents, such as bromovinyldeoxuridine, ganciclovir, and foscarnet, appeared equivalent to trifluridine or acyclovir. Oral acyclovir was equivalent to topical antiviral therapy and did not hasten healing when used in combination with topical treatment. Antiviral agents did not increase the speed of healing when compared to debridement but reduced the risk of recrudescent epithelial keratitis. The combination of physicochemical treatment with an antiviral agent seemed to be better than either physicochemical or antiviral treatment alone. The combination of topical interferon with an antiviral agent was significantly better than antiviral therapy [185].

Healthy practices to minimize CL related MK

Proper lens care practices help in reducing the CL associated MK. CDC recommendation of proper CL wear and eye health care includes, 1) washing hands with soap and water before wearing and removing CL, 2) Removing CL during sleep. Sleeping with CL on increases by 4 to 5 times the risk of susceptibility to MK [15], 3) Avoiding the use of CL while swimming or showering because most of the water bodies harbor microorganisms. 4) Rubbing and rinsing CL with a CL disinfecting solution only. Rubbing CLs with a clean finger and rinsing them with disinfecting solution is the most effective way to remove deposits and microbes from soft CLs [186]. 5) Replacement of CLs as recommended by doctors, because some CL wearers were reported poorer vision as a result of wearing CLs longer than indicated by their ophthalmologists [187]. 6) Rub and rinse your CL case also with CL disinfectant solution only, never use water. Biofilms in CL cases can be removed by rubbing and rinsing the case with disinfecting solution and wiping dry with a tissue [188,189]. 7) Do not top off solution (Do not mix the fresh solution with the old or used CL disinfectant solution). Topping off solution or mixing fresh solution with used solution in the case for storing CLs has been an important risk factor in serious outbreaks of CL associated infections [124]. Therefore, use only fresh CL disinfecting solution in the CL case.

CONCLUSION

Contact lenses may have advantages for some wearers, but improper care can cause serious eye infections. CL wear has been described as the most important predisposing factor for MK worldwide. Healthy contact lens wear and care awareness to the public is essential to minimize the MK in CL wearers. The theme of first annual Contact Lens Health Week November 17-21, 2014 is “You only have one pair of eyes, so take care of them”. Therefore one should follow healthy lens care practices to reduce the CL associated MK.

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