

Contact lens-associated microbial keratitis

Ceratitis microbianas relacionadas a lente de contato

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ABSTRACT

Purpose: Contact lens-associated microbial keratitis is a severe condition with sight-threatening potential and increasing incidence. Information regarding the etiological agents is essential in guiding management and may vary geographically. The aim of this study was to analyze the microbiological results of corneal scrapings collected from patients presenting with contact lens-associated microbial keratitis. **Methods:** Retrospective analysis of the records of all patients who were clinically diagnosed with contact lens-associated microbial keratitis and had corneal scrapings sent to the Laboratory of Ocular Microbiology, UNIFESP/EPM during a 5-year period from January 2002 to December 2007. **Results:** The etiological agent was identified in 239 patients. Bacterial isolates accounted for 166 (69.46%) cases, *Acanthamoeba* for 95 (39.75%) cases and fungi for 4 (1.67%) cases. Among the bacterial infections, coagulase-negative *Staphylococcus* was demonstrated in 74 cases, while *Pseudomonas* spp was found in 32 patients. All coagulase negative *Staphylococcus* and *Pseudomonas* were susceptible to ciprofloxacin and ofloxacin. Resistance to gentamicin was documented in a single case of *Pseudomonas*. Fourth-generation fluoroquinolone resistance was not observed among *Pseudomonas* cases. **Conclusion:** Coagulase-negative *Staphylococcus* was the most frequent isolate, and such data must be considered when determining empiric treatment. Second-generation fluoroquinolones ciprofloxacin and ofloxacin and fourth-generation fluoroquinolones moxifloxacin and gatifloxacin showed a good antibacterial profile and therefore could be good options for initial management.

Keywords: Contact lens/adverse effects; Keratitis/microbiology; Eye infections, bacterial; Corneal ulcer; *Acanthamoeba*

INTRODUCTION

The use of contact lenses (CL) has been widely associated with corneal alterations ranging in symptomatology and severity. Lesions may vary from small peripheral sterile infiltrates to infectious central ulcers with sight-threatening potential⁽¹⁻²⁾. Contact lens wear has been repeatedly described as the most important predisposing factor to microbial keratitis worldwide⁽³⁻⁴⁾, including Brazil⁽⁵⁾. The incidence of microbial keratitis has increased over the past decades accompanying a growing population of CL wearers⁽⁶⁾. The incidence of CL-associated microbial keratitis (CLMK) varies from 1.8 to 2.44 per 10,000 CL wearers/year⁽⁷⁾. Infections are more frequent in soft-lens users and the risk with gas-permeable rigid lenses is estimated to be one-third that with daily-wear soft lenses⁽⁸⁾. Extended wear is also associated with higher risk of microbial keratitis⁽⁹⁻¹¹⁾, while the impact of frequent replacement in reducing or increasing the incidence of infectious keratitis is still unclear⁽¹¹⁻¹²⁾.

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Most often, CLMK is related to bacterial infection, although *Acanthamoeba* and less frequently fungi can also be involved in the pathological process^(6-7,13-14). Bacterial keratitis is most commonly caused by aggressive gram-negative *Pseudomonas* spp. The bacterial agent seems to vary geographically according to climate and/or temperature. Temperate zones tend to have higher incidences of gram-positive and less aggressive keratitis⁽¹⁵⁾.

Amebic keratitis is a protozoal infection known to represent a severe condition with dramatic visual outcomes⁽¹⁶⁻¹⁷⁾ and to require a long and costly treatment⁽¹⁸⁾. The main risk factors for *Acanthamoeba* keratitis include failure to disinfect soft lenses, use of tap water to clean the lenses and the use of lenses while swimming^(7,19-20). Recently, confocal microscopy has been shown to be a valuable diagnostic tool, which could be especially helpful in cases with negative microbiological results despite clinical suspicion⁽²¹⁾.

Fungal infection was historically considered a rare form of CLMK and mostly associated with therapeutic CL⁽²²⁾, though some developing countries may have higher rates even among non-therapeutic contact-lens wearers⁽²³⁻²⁴⁾. Recent reports of *Fusarium* keratitis outbreaks among non-therapeutic CL users⁽²⁵⁻²⁶⁾, although partially attributed to a specific multipurpose solution, point to CL use as a growing risk factor for fungal keratitis⁽²⁷⁾.

The familiarity with the usual causative agents may help with the primary therapeutic choice. Several studies report the most frequent microbes involved in CLMK worldwide, but little data regarding the situation in Brazil is available. Considering the possible differences in CLMK agents according to regions and climate⁽¹⁵⁾, it is essential to gain knowledge of the most frequent agents of CLMK in our country.

The aim of our study was to analyze epidemiological data and microbiological results of all corneal scrapings collected from patients who were clinically diagnosed with CLMK during the period between January 2002 and December 2007 at the Laboratory of Ocular Microbiology, UNIFESP/EPM.

METHODS

We analyzed retrospectively the records of all patients who were clinically diagnosed with CLMK and had corneal scrapings sent to the Laboratory of Ocular Microbiology, UNIFESP/EPM during the 5-year period of January 2002 to December 2007. The following data were collected: gender, age, type of lens used (soft or hard), microbiological results including microscopic analysis and culture growth in different media of the corneal scrapings and also CL culture. All the scrapings were performed according to the standard routine of the Laboratory of Ocular Microbiology-UNIFESP/EPM. Scrapings were always performed by a trained physician using slit lamp, Kimura scalpel, and topical anesthesia. Corneal material was smeared on 2 slides and stained with Giemsa and Gram stains. Corneal material was also added to

thioglycollate (Thio) broth, brain-heart-infusion (BHI) broth, Sabouraud glucose agar plate, blood agar plate and chocolate agar plate, to test for microbial growth. Additional slide staining and/or culture media were used depending on the clinical suspicion. Non-nutrient agar with an overlay of *Escherichia coli* media, for example, was always used when *Acanthamoeba* infection was clinically suspected. On the other hand, fewer media and/or slides were used if only little material could be obtained.

RESULTS

During the period of January 2002 to December 2007, 2455 corneal scrapings were analyzed at the Laboratory of Ocular Microbiology, UNIFESP/EPM with the clinical diagnosis of infectious keratitis. Three hundred sixty-six (14.91%) patients were CL users and among them, 239 had culture-proven microbial keratitis and were included in the study.

Mean age was 29.75 years (ranging from 9 to 84 years) and the male to female ratio was 1:1.26.

Bacterial agent accounted for 166 cases (69.46%), while *Acanthamoeba* was verified in 95 patients (39.75%) and fungus was isolated in 4 cultures (1.67%). The causative organisms are shown in Table 1.

Table 1. Causative agents in culture-proven cases of contact lens-related microbial keratitis

Microbiological agent	n
Gram-positive bacteria	110 (41.20%)
Coagulase-negative <i>Staphylococcus</i>	74
<i>Corynebacterium</i> spp	20
<i>Staphylococcus aureus</i>	10
<i>Streptococcus</i> spp	4
Other gram-positive bacteria	2
Gram-negative bacteria	58 (21.72%)
<i>Pseudomonas</i> spp	32
<i>Pseudomonas aeruginosa</i>	13
<i>Pseudomonas fluorescens</i>	4
<i>Serratia</i> spp	15
<i>Enterobacter aerogenes</i>	5
<i>Klebsiella</i> spp	1
<i>Proteus mirabilis</i>	1
<i>Citrobacter freundii</i>	1
<i>Achromobacter xyloxidans</i>	1
<i>Alcaligenes</i> spp	1
<i>Moraxella</i> spp	1
<i>Acanthamoeba</i>	95 (35.58%)
Fungus	4 (1.50%)
<i>Candida</i> spp	3
<i>Aureobasidium pullulans</i>	1
Total isolated agents*	267 (100%)

* Two patients had polybacterial keratitis, with *Pseudomonas* spp and *Serratia* spp isolated in both cases, 25 patients had amebic and bacterial co-infection and 1 case had fungal and bacterial co-infection

The type of lens used was available from patient charts in 109 of the 166 cases of bacterial keratitis. Ninety-six patients were soft-lens wearers (88.07%), 11 were rigid gas-permeable lens wearers (10.09%) and 2 used piggy-back lenses (1.83%). Among the 96 soft-lens wearers, there were 3 cases of therapeutic CL use and 8 cases of cosmetic lens use. Four of the 8 cosmetic CL wearers were using lenses from another person at the time of the infectious event.

In 36 patients with culture-proven bacterial keratitis, inadequate lens hygiene was documented on the charts. Nineteen of them used mostly saline solution while cleaning the lenses and 3 used tap water. Lens wear in the shower was recorded in 15 cases and while swimming in 16 cases. Overnight lens use was noted in 19 of the cases of bacterial keratitis.

Gram-positive bacteria were observed in 110 patients, corresponding to 41.20% of all the examinations with identified etiological agent and to 66.26% of all the examinations with a bacterial agent. Gram-negative bacteria were noted in 58 of the cases (21.72% of all the examinations with identified etiological agent and 34.94% of all the examinations showing a bacterial agent).

In the gram-positive group, the most frequent agent was coagulase-negative *Staphylococcus* (CoNS), which was found in 74 patients (27.71%). *Corynebacterium* spp was present in 20 (7.49%) of the examined cultures.

Pseudomonas spp was the most common gram-negative etiological agent and was isolated in 32 (11.98%) cases. *Pseudomonas aeruginosa* was the most common species of the genus (13 of 32 patients). *Serratia* spp was isolated in 15 cases and *Enterobacter aerogenes* in 5 cases. Other gram-negative bacteria found are listed in Table 1. Polybacterial infection was documented in 2 cases, both with association of *Pseudomonas* spp and *Serratia* spp.

Coagulase-negative *Staphylococcus* was susceptible to cephalotin and oxacillin in all 74 cases. No cases of resistance to vancomycin were observed. The second-generation fluoroquinolones ciprofloxacin and ofloxacin were tested in 57 cases, all of them showing susceptibility. Fourth-generation fluoroquinolones were not tested in all cases due to their lack of availability by the time of the examination. Moxifloxacin and gatifloxacin responses were examined in 65 of the 74 cases of CoNS. Resistance was observed in 2 cases: one of them to both moxifloxacin and gatifloxacin and the other only to gatifloxacin. Susceptibility to amikacin, gentamicin and tobramycin was tested in 58, 56 and 52 cases, respectively. No cases of resistance to such aminoglycosides were documented.

In all the 32 cases of *Pseudomonas* spp, the antibiogram demonstrated susceptibility to ciprofloxacin. Ofloxacin was tested in 29 cases with no cases of resistance. Sensitivity to gatifloxacin was accessed in 23 cases of the cultured *Pseudomonas* spp and the bacteria showed to be susceptible to this drug in all the tested cases. In regard to aminoglycosides sensitivity, in all of the 32 *Pseudomonas* cases, the bacteria were sensitive to amikacin and tobramycin. Resistance was observed in one case to gentamicin and in 3 cases to neomycin.

Acanthamoeba was present in 95 (39.75%) patients, of whom 25 (26.31%) had bacterial co-infection. Bacterial agents associated with *Acanthamoeba* infection are shown in Table 2. In 13 (13.68%) of the cases of *Acanthamoeba* keratitis, the patient was taking antiviral drugs, considering the possibility of herpes infection. Data regarding the type of lens used by the patients with amebic keratitis was recorded in 60 cases, among which 52 (86.67%) were soft lenses and 8 (13.33%) were rigid gas-permeable lenses. Information on lens care and shower and swimming habits was available in 51 charts. Thirty patients reported inadequate lens hygiene. Twenty-three of them used mainly physiologic saline to clean the lenses and 7 used tap water. Eight patients stated wearing their lenses while showering and 12 while swimming. Only one patient used lenses overnight.

Fungi were noted in 4 (1.67%) of all the cases. In 3 cases, the isolate was a yeast (*Candida* spp), while in one case it was a filamentous fungus (*Aureobasidium pullulans*). One of the patients with *Candida* keratitis had CoNS co-infection.

Culture of CL was performed in 30 cases of laboratory-proven bacterial keratitis and in 13 cases of amebic keratitis. In the 30 cases of bacterial keratitis, the CL culture was positive in 22 examinations, among which 10 (45.45%) demonstrated growth of the same bacterium as in corneal scraping cultures and 12 (54.55%) did not. In 7 cases, the lens culture was positive for *Acanthamoeba*, while corneal material showed bacterial growth and provided no evidence of protozoal eye infection. Among the 13 cases of corneal scraping culture-proven *Acanthamoeba* keratitis, CL culture led to the isolation of the protozoa in 6 cases (46.15%) and showed no growth in 7 cases (53.85%). Nine (20.93%) of the total 43 CL cultures displayed polymicrobial growth.

DISCUSSION

Several studies have presented consistent data pointing to *Pseudomonas* as the leading agent in bacterial keratitis in CL users^(13,15,28). The results of the present study showed a higher prevalence of CoNS. Coagulase-negative *Staphylococcus* are among the most frequently isolated bacteria in the clinical microbiology laboratory. Since such bacteria are normal inhabitants of human skin and mucosae, differentiation between clinically significant CoNS and contaminant

Table 2. Bacterial agents involved in *Acanthamoeba* co-infection cases

Bacterial agent	n
Coagulase negative <i>Staphylococcus</i>	20 (80%)
<i>Corynebacterium</i> spp *	3 (12%)
<i>Streptococcus viridans</i>	1 (4%)
<i>Serratia</i> spp	1 (4%)
Total	25 (100%)

* *Corynebacterium xerosis* was identified in 2 cases

strains is a challenging task. Considering the meticulous scraping technique followed as a routine in the study, however, the shown high prevalence of CoNS point to CoNS as a main CLMK agent in our environment.

Oxacillin resistance was not found among CoNS in the present study, though increasing prevalence has been observed among general eye infections in Brazil⁽²⁹⁻³¹⁾. Oxacillin resistance is used to evaluate the resistance of *Staphylococcus* to beta-lactam agents. Resistance to oxacillin and/or methicillin is directly associated with resistance to all beta-lactam drugs, such as cephalosporins and carbapenems⁽³²⁾. It is thus reasonable to avoid beta-lactam drugs in cases of oxacillin-resistant CoNS, even if they show satisfactory susceptibility to these drugs *in vitro*.

As for the gram-negative *Pseudomonas*, resistance to one of the aminoglycoside drugs does not necessarily predict resistance to other drugs of the same class⁽³³⁾. In our study, *Pseudomonas* resistance to tobramycin and gentamicin was observed in a single case, while no case of amikacin resistance was noted.

Standard empiric therapy for bacterial keratitis has been historically based on the combination of fortified eye drops of cephalosporin and aminoglycoside drugs. In the present study, second-generation fluoroquinolones ciprofloxacin and ofloxacin and fourth-generation fluoroquinolones moxifloxacin and gatifloxacin displayed satisfactory rates of susceptibility to both gram-positive and-negative bacteria. Hyn-diluk et al. compared clinical response to ciprofloxacin 0.3% and tobramycin-cephazolin in cases of bacterial keratitis and found equal results⁽³⁴⁾. Constantinou et al. also found similar clinical response when comparing moxifloxacin, ofloxacin and fortified tobramycin-cephazolin in the treatment of bacterial keratitis⁽³⁴⁾. Fluoroquinolones are easily available commercially, since they do not require preparation, and the use of such drugs could be a good choice for initial empiric treatment for CLMK. Considering the higher prevalence of CoNS than *Pseudomonas*, the use of fourth-generation fluoroquinolones may have a better efficiency than second-generation fluoroquinolones. It is prudent to scrape the cornea before prescribing antibiotics and reconsider treatment options following clinical response and microbiological results.

In this study, there were 95 (39.75%) cases of culture-proven *Acanthamoeba* keratitis. Previous studies found lower rates of *Acanthamoeba* infection, with a prevalence ranging from zero to 3.2% of infectious keratitis from contact lens wear^(13,15). This high prevalence can be an indication of unsatisfactory quality of home water system and poor lens care habits. It is also important to consider that the study was conducted in a tertiary Ophthalmology service, which receives more severe cases. Clinical features of *Acanthamoeba* keratitis is variable and can be mistaken for herpes infection⁽³⁵⁾. In our data, 13 of the 95 patients (13.68%) with positive culture to *Acanthamoeba* were being treated for herpes keratitis. Owing to the drastic visual loss potentially associated with ameba eye infection and the impact of early diagnosis and treatment, it is

essential to consider testing for *Acanthamoeba* infection even when clinical features point to herpetic etiology, especially considering the lack of consistent data supporting an association between viral infection and CL use.

Fungal infection was found in a minority of the patients (1.67%), confirming previous literature findings^(7,13,36). In 2006, there was a growing number of reports of *Fusarium* keratitis that was associated with the use of a specific ReNu[®] (Bausch & Lomb) product with MoistureLoc[®] (Bausch & Lomb). Such association became even more evident after the decline in CL-related *Fusarium* reports following the recall of the product⁽²⁵⁾. Other ReNu[®] (Bausch & Lomb) products without the MoistureLoc[®] (Bausch & Lomb) component are commercially available worldwide and also in Brazil, and had not been associated with fungal keratitis.

Despite previous studies supporting a strong association between corneal scrapings and CL cultures⁽³⁷⁻³⁸⁾, our results point to a poor agreement. In addition, we found multiple isolates in the CL culture more frequently than in the corneal culture. Such data highlight the notion that the positivity of a CL culture does not always mean corneal infection. The clinical importance of CL culture still remains uncertain, and such information must be pondered with caution for both diagnosis and treatment options.

RESUMO

Objetivo: A ceratite microbiana associada ao uso de lente de contato é uma condição clínica grave, com risco de perda visual e cuja incidência vem aumentando progressivamente. Os principais agentes etiológicos podem variar geograficamente e informações referentes aos agentes causais são essenciais para tratamento apropriado. Este estudo se propõe a analisar os resultados microbiológicos de raspados de córnea coletados de pacientes usuários de lente de contato com quadro de ceratite microbiana. **Métodos:** Foi realizada análise retrospectiva de todos os estudos microbiológicos de pacientes usuários de lente de contato com diagnóstico clínico de ceratite microbiana que tiveram material corneal enviado para o Laboratório de Microbiologia Ocular UNIFESP durante o período de 5 anos de janeiro de 2002 a dezembro de 2007. **Resultados:** Dos 239 pacientes em que foi possível identificação, o agente era bactéria em 166 (69,46%), *Acanthamoeba* em 95 (39,75%) e fungo em 4 (1,67%). *Staphylococcus* coagulase negativo foi encontrado em 74 casos, dos quais todos eram sensíveis tanto a ciprofloxacino quanto a ofloxacino. Dois casos de resistência a quinolonas de quarta geração (gatifloxacino e moxifloxacino) foram identificados entre os casos de *Staphylococcus* coagulase negativo. *Pseudomonas* spp foi isolada em 32 pacientes, dos quais todos eram sensíveis a quinolonas de segunda geração (ciprofloxacino e ofloxacino) e de quarta geração. Foi encontrado um único caso de *Pseudomonas* resistente a gentamicina. **Conclusão:** *Staphylococcus* coagulase negativo foi isolado em um número de casos superior a *Pseudomonas*, o

agente tradicionalmente considerado o principal de ceratites microbianas associadas ao uso de lente de contato. Aminoglicosídeos, fluorquinolonas de segunda e de quarta geração apresentaram um perfil antibiótico satisfatório para o tratamento empírico de ceratites microbianas em usuários de lente de contato.

Descritores: Lentes de contato/efeitos adversos; Ceratite/microbiologia; Infecções oculares bacterianas; Úlcera de córnea; *Acanthamoeba*

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