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Original Article

Etiological and Clinical Features of Contact Lens-Associated Microbial Keratitis

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Abstract

Objectives: To determine the demographic, etiological, microbiological, and clinical characteristics and present treatment results of contact lens (CL)-associated microbial keratitis (CLAMK).

Materials and Methods: Medical records of patients who were followed in our clinic for CLAMK between January 2014 and May 2020 were retrospectively analyzed. Demographic characteristics, symptom duration, CL and usage characteristics, risk factors, isolated microorganisms, lesion characteristics, hospital stay, recovery and follow-up times, and best corrected visual acuities (BCVA) at first and last examination were recorded.

Results: The 22 patients (16 females, 6 males; 22 eyes) had a mean follow-up time of 13.0±18.3 months and mean age of 26.9±14.3 years. Most of the female patients (13/16) were under 35 years old. At least one risk factor associated with improper CL usage was identified in 21 patients (95.4%). The most common risk factor was sleeping with CL (n=15, 68.1%). Causative microorganisms were detected on microbiological examination in 15 cases (68.1%). The most common microorganism was *Pseudomonas aeruginosa* (n=8). Causative pathogens were sensitive at rates of 84.2%, 95% and 94.7% to combined vancomycin/amikacin, combined vancomycin/ceftazidime, and moxifloxacin, respectively. Mean BCVA was 0.9±1.1 logMAR in the first examination and increased to 0.59±1.1 at last examination (p=0.006). There was a negative correlation between BCVA at presentation and length of hospital stay (p=0.014).

Conclusion: Mistakes in CL use are a frequent predisposing factor in patients with CLAMK. Informing CL users in detail about CL usage and cleaning may reduce the frequency of these mistakes and thus infections. Current antibiotic options that should be preferred in empirical treatment remain largely effective against likely pathogens. Favorable visual outcomes can be obtained in most cases with detailed diagnostic examination and appropriate treatment approaches.

Keywords: Contact lenses, mistakes related to contact lens use, contact lens-associated microbial keratitis, microbial keratitis, pseudomonas

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Introduction

Microbial keratitis (MK) is one of the leading causes of unilateral blindness worldwide. While trauma is the most common cause of MK in developing countries, contact lens (CL) use is predominant in developed countries.[1] In addition to this difference in the etiology of MK, the incidence of CL-associated corneal infections has increased in all countries in recent years.[2,3] In these infections, which are the most serious and sight-threatening complications of CL use, gram-negative bacteria (especially *Pseudomonas aeruginosa*) can cause severe clinical pictures that may even require keratoplasty.[1,4,5] Mistakes in lens use and care have a prominent role in CL-related MK.[2] Patients often have various risk factors, such as the acquisition and use of CLs without a prescription, neglect of hand hygiene during CL insertion and removal, sleeping, showering, and swimming with CLs, and inappropriate cleaning of CLs and CL cases.[2,6,7] Challenges in the diagnosis and treatment of the disease and the aggressive pathogens and various risk factors involved increase the importance of the results reported from different reference centers in terms of preventing these infections and improving their management.

This study aimed to determine the demographic, etiological, microbiological, and clinical characteristics of CL-related MK patients who presented to a tertiary reference center over a 6-year period and present their treatment outcomes.

Materials and Methods

The medical records of patients who were followed for CL-related MK in our clinic between January 2014 and May 2020 were reviewed retrospectively. MK cases associated with the use of therapeutic CLs were not included in the study. Approval for the study was obtained from the Çukurova University Faculty of Medicine Ethics Committee (decision number: 19, meeting number and date: 108/12.02.2021) and the study was conducted in accordance with the principles of the Declaration of Helsinki. Demographic characteristics, symptom duration, details regarding CL material, care, and use, risk factors, the microorganism(s) isolated, lesion characteristics, presence of hypopyon, length of hospital stay, recovery time, follow-up time, and best corrected visual acuity at initial presentation and last examination were recorded for all patients. Infiltrate location was noted as central, paracentral, and peripheral. Infiltrate depth was evaluated biomicroscopically and classified as superficial (less than 2/3 of corneal thickness) or deep (more than 2/3 of corneal thickness).

Microbial Analysis

The diagnosis was made by in vivo confocal microscopy in one patient with infiltrate in the anterior stroma and no epithelial defect. In another patient whose corneal lesion was superficial and outside the visual axis, only corneal swab culture was obtained. In all cases except these two patients, both the base and margins of the infiltrates were scraped under topical anesthesia and the samples were 1) examined by direct microscopy for bacteria, fungi, and *Acanthamoeba*, and 2) inoculated onto appropriate bacterial and fungal culture media: blood agar (bioMérieux, Marcy l'Etoile, France), chocolate agar (bioMérieux), Sabouraud dextrose agar (Merck; Darmstadt, Germany), brain-heart infusion agar (bioMérieux), and thioglycolate liquid medium (bioMérieux). 3) For *Acanthamoeba* culture, 2% non-nutrient agar was prepared and sterilized by autoclave, then distributed into sterile petri dishes. The petri dishes containing solid agar medium were incubated at 37 °C and examined for contamination. *Escherichia coli* was then spread over the entire surface of the agar. Corneal abrasion material in sterile saline was added to the *E. coli*-coated surface and incubated at 27 °C for 1 week. Samples from the medium were then examined under 400X magnification using a light microscope.[8] The presence of *Acanthamoeba* was also examined by polymerase chain reaction (PCR) test. 4) The presence of herpes simplex virus was investigated by immunohistological staining and light microscope examination of corneal samples and by PCR test. When they could be obtained, the lenses, lens solutions, and cases used by the patients were also sent for microbiological analysis to identify microorganisms by direct examination and cultures. Identification and antibiotic susceptibility testing of bacterial species were performed with the VITEK 2 system (bioMérieux).

In all cases of MK, initial treatment was empirical. Empirical topical therapy consisted of moxifloxacin (0.5%; Vigamox, Alcon, Fort Worth, USA) or combined fortified vancomycin (50 mg/mL; Koçak, İstanbul, Turkey) and amikacin (50 mg/mL; Osel, İstanbul, Turkey), depending on clinical severity. In patients with fungal pathogens detected in cytological examination and/or culture, hourly topical antifungal treatment was added (fortified voriconazole [10 mg/mL; Vfend, Pfizer, New York, USA] or amphotericin B [2.5 mg/mL; AmBisome, NeXstar Pharmaceuticals, San Dimas, USA] [if *Aspergillus* species or yeast infection was detected]). In the presence of *Acanthamoeba*, 0.02% chlorhexidine drops and, when obtainable, 0.1% propamidine isethionate (Brolene, Sanofi-Aventis, Bridgewater, NJ, USA) drops were added to treatment. In all cases, 1% cyclopentolate eye drops (Siklopleji̇n, Abdi İbrahim, Turkey) were administered 1-3 times a day. The subsequent treatment protocol was determined according to clinical response and the results of microbial examinations. In cases of polymicrobial keratitis, treatment was modified to target all identified pathogens. For all patients, the frequency and duration of treatment were determined according to the clinical response observed during follow-up. If medical treatment was insufficient, various additional treatments were used: intrastromal injection, corneal cross-linking, amniotic membrane transplantation (AMT), and penetrating keratoplasty (PK).

Statistical Analysis

IBM SPSS Statistics Version 20.0 software package was used for statistical analyses.[9] Categorical parameters were summarized as number and percentage, and numerical parameters as mean

and standard deviation (with median and minimum-maximum where necessary). The Wilcoxon signed-rank test was used to compare two non-normally distributed dependent numerical measurements. Level of significance was accepted as 0.05 for all tests.

Results

The study included 22 eyes of 22 patients with CL-related MK (16 females [72.7%], 6 males [27.3%]). Although the mean age was 26.9±14.3 years (range: 1.5-76), the majority of the female patients (13/16, 81.2%) were under the age of 35. The infection affected the right eye in 10 patients and the left eye in 12 patients. The cases were evenly distributed over the years. When evaluated by season, it was seen that most of the patients presented in autumn (n=9, 40.9%) and winter (n=6, 27.3%). Five patients (22.7%) first presented in summer and 2 (9.1%) presented in spring. One patient had diabetes mellitus (DM); the other patients had no ocular surface-related or systemic pathology that would predispose to corneal infection. Four patients had a history of smoking and 2 patients had a history of previous CL-related infection. All patients but one were referred to our clinic from other centers. Eighteen patients were using CLs by physician prescription, and 4 patients said they obtained CLs from an optician. All patients were using soft CLs. Lens material was silicone hydrogel in 16 cases (72.7%), hydrogel in 2 cases (9%), and silicone elastomer in 1 pediatric aphakic patient (4.5%). CL material information could not be obtained for the other 3 patients. Nineteen patients used daily wear-frequent replacement CLs, and one pediatric patient used an extended-wear CL (6 nights). Data on wear regimen could not be obtained in two cases. CL use was bilateral in all patients except one pediatric patient, and was for cosmetic purposes in 3 patients (13.6%) and refractive purposes in the remaining patients (spheric CL in 12, toric CL in 7 patients). Mean duration of CL use was 49.3±36.1 months (range: 1-144) and the mean daily wear time was 12.3±3.5 hours (range: 7-24). Risk factors related to CL use and clinical characteristics of the patients are shown in Table 1. The most common risk factor associated with CL use was sleeping with CLs (n=15, 68.1%). Other common risk factors included extending the recommended CL replacement interval (n=6, 27.2%) and showering with CLs (n=5, 22.7%) (Table 1).

The causative microorganism could be detected in 15 cases (68.1%). In the patient with anterior stromal infiltrate and no epithelial defect, the diagnosis of *Acanthamoeba* keratitis was made by in vivo confocal microscopy. In the other 14 patients, the causative pathogens were detected by microbiological examination of corneal specimens (Table 2). Five patients (22.7%) provided CL-related materials for microbial examination. Pathogens were detected by microbial examination of samples obtained from the CL case in 3 cases and from the CL in 2 cases (Table 2). Bacterial infection was detected in 7 cases (31.8%), fungal infection in 1 case (4.5%), and parasitic infection in 1 case (4.5%). Six patients (27.2%) had polymicrobial infections: bacterial/fungal in 3 cases (Figure 1A-C), bacterial/*Acanthamoeba* in 2 cases (Figure 2A-D), and bacterial/fungal/*Acanthamoeba* in 1 case (Table 2). Four patients (3 female, 1 male; cases 2, 4, 12, and 15; Table 2) aged 14-42 years stated that they obtained CLs from an optician. When these patients were evaluated in terms of risk factors associated with CL use (Table 1), they were found to have 1 (n=1), 2 (n=2), or 4 (n=1) different risk factors. Etiology was bacterial in 1 of these patients, parasitic in 1 patient, and polymicrobial in the other 2 patients (bacterial/fungal in both cases) (Table 2).

All bacterial and fungal pathogens in our patients were demonstrated by culture analysis. In two of the fungal infections, cytological examination supported the diagnosis. In all cases except for one diagnosed by confocal microscopy, *Acanthamoeba* diagnosis was made by PCR analysis. The majority of bacterial isolates were gram-negative pathogens (18/23, 78.2%). The most commonly isolated bacteria were *P. aeruginosa* (8/23, 34.7%). The susceptibility patterns of the bacterial isolates to antibiotics frequently preferred in empirical treatment are shown in Table 3. Bacterial agents had susceptibility rates of 84.2% to combined vancomycin-amikacin, 95% to combined vancomycin-ceftazidime, and 94.7% to moxifloxacin (Table 3).

Table 1. Risk factors and clinical features associated with contact lens use

Risk factors, n (%)	
Sleeping with CL†	15 (68.1%)
Delaying CL replacement	6 (27.2%)
Showering with CL	5 (22.7%)
Smoking	4 (18.1%)
Swimming with CL	3 (13.6%)
Washing CL and CL case with tap water	3 (13.6%)
Not changing CL solution daily	3 (13.6%)
Diabetes mellitus	1 (4.5%)
Symptom duration (days)	13.0±21.3 (1-90)
Pre-treatment BCVA‡ (logMAR)	0.9±1.1 (0-3.1)
Infiltrate location, n (%)	
Central	8 (36.3%)
Paracentral	7 (31.8%)
Peripheral	7 (31.8%)
Lesion depth, n (%)	
Deep	6 (27.2%)
Superficial	16 (72.7%)
Presence of hypopyon, n (%)	4 (18.1%)
Lesion size (mm^2)	9.11±15.4 (0.2-53.2)
Recovery time (days)	14.3±7.5 (5-60)
Mean follow-up time (months)	
Post-treatment BCVA‡ (logMAR)	

CL: Contact lens, BCVA: Best corrected visual acuity, †: The pediatric patient prescribed an extended wear regimen was not included in the analysis, ‡: Could not be measured in one pediatric patient

Table 2. Culture results and treatments administered to patients with detectable pathogens

Case	Age (years)	Eye	Sex	Corneal scraping	Contact lens	Lens case	Lens solution	Topical therapy	Additional therapies
1	15	Right	Female	*Pseudomonas aeruginosa*	-	*Candida* non-*albicans*	No growth detected	F. ceftazidime F. voriconazole	Intrastromal voriconazole
2	18	Right	Female	*Serratia marcescens* Yeast	*Serratia marcescens* *Stenotrophomonas maltophilia*	-	No growth detected	Moxifloxacin F. amphotericin B, Chlorhexidine[§]	None
3	24	Right	Female	*Pseudomonas aeruginosa* *Klebsiella oxytoca*	-	-	-	Moxifloxacin	None
4	22	Right	Male	*Staphylococcus epidermidis*	-	-	-	Moxifloxacin, Chlorhexidine[&]	None
5	34	Left	Female	*Viridans* group *streptococcus*	-	-	-	F. vancomycin F. amikacin	None
6	19	Right	Female	*Alcaligenes faecalis* *Klebsiella oxytoca* *Pseudomonas aeruginosa*	-	-	-	F. amikacin Moxifloxacin	None
7	51	Left	Female	*Aspergillus flavus*	-	-	-	F. voriconazole F. amphotericin B, Chlorhexidine[§], Moxifloxacin[¶]	Oral voriconazole Intrastromal voriconazole, PK
8	20	Left	Male	*Pseudomonas aeruginosa*	No growth detected	*Acanthamoeba*[†]	No growth detected	F. piperacillin-tazobactam F. gentamicin Chlorhexidine, Moxifloxacin	None
9	23	Left	Female	*Trichosporon mucoides,* *Staphylococcus epidermidis* *Acanthamoeba*[†] *Aspergillus flavus*	-	-	-	F. amphotericin B, F. caspofungin, Chlorhexidine	Oral ketoconazole Intrastromal voriconazole, CXL
10	33	Left	Female	*Pseudomonas aeruginosa* *Delftia acidovorans* *Achromobacter xylosoxidans*	-	-	-	F. ceftazidime Moxifloxacin	None
11	21	Left	Female	*Micrococcus species* *Acanthamoeba*[†]	-	-	-	F. polymyxin B+, Trimethoprim, Chlorhexidine	None
12	14	Left	Female	*Pseudomonas aeruginosa* *Candida* non-*albicans* *Acinetobacter haemolyticus*	*Acinetobacter haemolyticus,* *Pseudomonas aeruginosa,* *Shewanella putrefaciens*	-	-	F. amikacin F. amphotericin B, Moxifloxacin	AMT
13	1.5	Left	Male	*Pseudomonas aeruginosa* *Staphylococcus epidermidis*	-	*Pseudomonas aeruginosa* *Serratia marcescens*	No growth detected	F. gentamicin, Moxifloxacin	None
14	30	Right	Male	*Pseudomonas aeruginosa* *Serratia marcescens* *Stenotrophomonas maltophilia*	-	-	-	F. amikacin Moxifloxacin	None
15	42	Left	Female	*Acanthamoeba*[‡]	-	-	-	Chlorhexidine Dibromopropamidine	None

F: Fortified, PK: Penetrating keratoplasty, CXL: Corneal crosslinking, AMT: Amniotic membrane transplantation. [†]: Diagnosis was made by polymerase chain reaction method, [‡]: Diagnosis was made by confocal microscopy, [§]: Chlorhexidine was initiated for suspected *Acanthamoeba* keratitis based on medical history and clinical findings. After the detection of fungal pathogens, chlorhexidine was also continued in addition to antifungal drugs because of its antifungal effect; [&]: Chlorhexidine was administered for presumed *Acanthamoeba* keratitis based on medical history and atypical clinical presentation. [¶]: Polymicrobial etiology could not be excluded because the infiltrate was large and deep, and topical antibiotic treatment was continued.

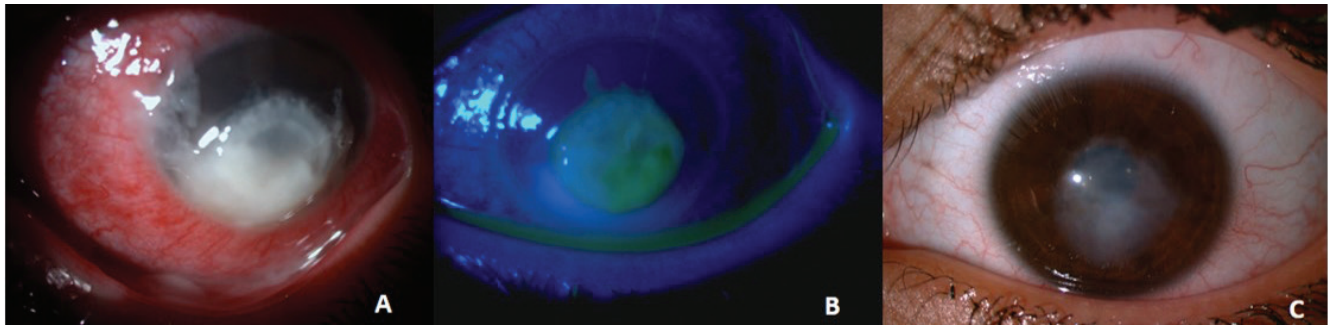

Figure 1. A 14-year-old girl using cosmetic contact lenses for 2 years presented with complaints of whiteness in her left eye, loss of vision, and pain for 2 days. Vision was at the level of light perception. A) Anterior segment photograph at first presentation shows a central corneal infiltrate 6.8x6.4 mm in size with feathery borders and hypopyon in the inferior. B) At first presentation, the infiltrate is stained with fluorescein under cobalt blue light. Corneal scraping cultures yielded *Pseudomonas aeruginosa, Acinetobacter haemolyticus,* and *Candida* non-*albicans,* while *Shewanella putrefaciens* was also isolated from samples taken from the contact lens. C) At 6 months after treatment, the infiltrate is healed with scarring. The patient's visual acuity increased to counting fingers at 4 meters and keratoplasty was planned.

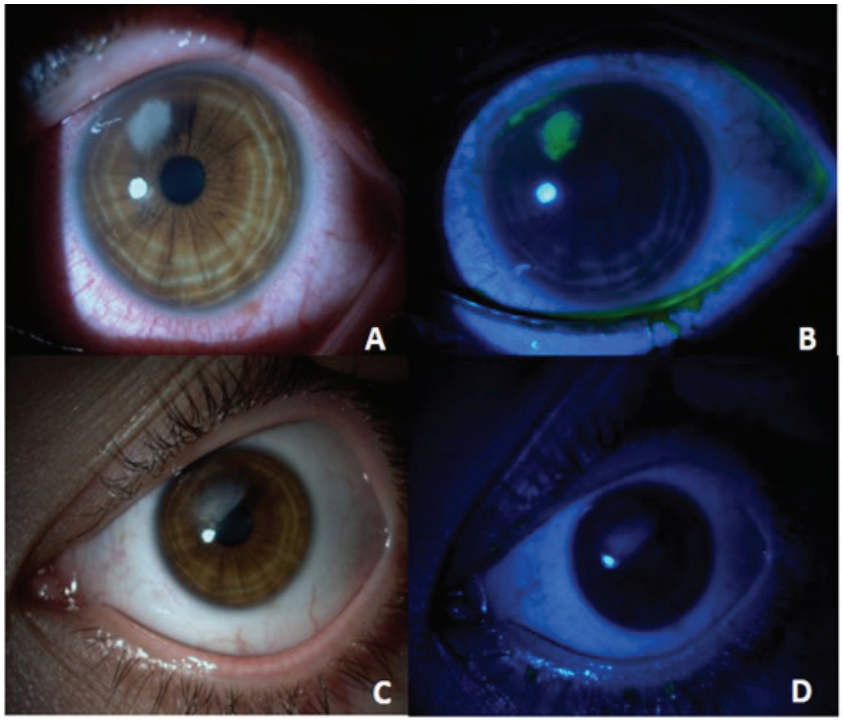

Figure 2. A 20-year-old man with a 4-month history of using soft silicone hydrogel spheric contact lenses for refractive purposes presented with complaints of stinging in his left eye for 2 days. The patient reported washing his contact lenses and lens case with tap water. A) The anterior segment photograph at first presentation shows a 2.3x2.7 mm paracentral corneal infiltrate in the superotemporal region in the left eye. B) At first presentation, the infiltrate is stained with fluorescein under cobalt blue light. Corneal scraping culture yielded *Pseudomonas aeruginosa* and *Acanthamoeba* was detected in samples taken from the lens case. C) At 3 months after treatment that infiltrate is healed with scarring. D) The epithelial defect over the infiltrate is closed with no fluorescein staining.

Thirteen patients (59%) received only topical antimicrobial therapy (Table 2). In addition to the general principles specified above in the methods section, topical therapy was modified according to medical history and clinical findings in some patients (cases 2, 4, and 7) (Table 2). In addition to topical antifungal therapy, patients with fungal pathogens were additionally treated with intrastromal antifungal injection (n=3), systemic antifungal therapy (n=2), and corneal cross-linking therapy (n=1) (Table 2). After these treatments, the infiltrate completely disappeared and clinical improvement was achieved in 17 patients (17/19, 89.5%) with a mean follow-up period of 13±18.3 months. One patient found to have *Aspergillus flavus* underwent AMT followed by tectonic PK, and another patient with no pathogen identified by microbial examinations also underwent tectonic PK (total 2 patients with PK; 2/19, 10.5%). Three patients were lost to follow-up during the treatment process. Nineteen patients were treated on an inpatient basis, while 3 underwent outpatient treatment and follow-up. The mean length of hospital

Table 3. Sensitivity patterns of isolated bacteria to antibiotics frequently preferred in empirical treatment

Case	Pathogen	Resistance (MIC-3/zone mm)			
		Vancomycin	Amikacin	Ceftazidime	Moxifloxacin
1	*Pseudomonas aeruginosa*	-	S (≤2)	S (2)	S (≤0.25)
2	*Serratia marcescens*	-	S (≤2)	S (≤0.12)	S (≤0.25)
3	*Pseudomonas aeruginosa*	-	S (≤2)	S (2)	S (≤0.25)
	Klebsiella oxytoca	-	S (≤2)	S (≤0.12)	S (≤0.25)
4	*Staphylococcus epidermidis*	-	-	-	S†
5	*Viridans group streptococcus*	S (0.5)	-	-	-
6	*Alcaligenes faecalis*	-	-	S (2)	S (1)
	Klebsiella oxytoca	-	S (≤2)	-	S (≤0.25)
	Pseudomonas aeruginosa	-	S (≤2)	S (2)	-
8	*Pseudomonas aeruginosa*	-	R (16)	I (16)	R (≥4)
9	*Staphylococcus epidermidis*	S (1)	-	-	S (≤0.25)
10	*Pseudomonas aeruginosa*	-	-	S (2)	S (≤0.25)
	Delftia acidovorans	-	R (≥64)	S (2)	I (1)
	Achromobacter xylosoxidans	-	R (≥64)	S (2)	I (1)
11	*Micrococcus* spp.	S†	-	-	S†
12	*Pseudomonas aeruginosa*	-	S (≤2)	S (4)	S (≤0.25)
	Acinetobacter haemolyticus	-	S (≤2)	S (4)	S (≤0.25)
13	*Pseudomonas aeruginosa*	-	-	S (2)	-
	Staphylococcus epidermidis	S (1)	-	-	S (≤0.5)
	Serratia marcescens	-	I (2)	S (0.25)	S (≤0.25)
14	*Pseudomonas aeruginosa*	-	S (≤2)	S (2)	S (≤0.25)
	Serratia marcescens	-	S (≤2)	S (0.25)	S (≤0.25)
	Stenotrophomonas maltophilia	-	-	-	-

MIC: Minimal inhibitory concentration, S: Sensitive, I: Intermediate, R: Resistant, †: MIC value could not be determined

stay for the 19 inpatients was 7.9±7.5 days (range: 3-30) and there was an inverse correlation between visual acuity at initial admission and length of hospital stay (p=0.014). There was no significant relationship between other demographic and clinical parameters recorded at first admission and treatment outcome parameters (length of hospital stay, corneal epithelialization time, visual improvement after treatment) (p>0.05 for all).

Level of vision at initial presentation was hand movements in 4 patients, counting fingers at 1-5 meters in 4 patients, 0.1-0.5 decimal in 6 patients, and 1.0 decimal in 7 patients (visual acuity could not be measured in one pediatric patient). Vision was unchanged after treatment in the latter 7 patients, and improved by 1 line or more in 10 (71.4%) of the other 14 patients. Post-treatment visual acuity was unchanged in 3 patients (21.4%) and decreased in 1 patient (7.1%). Mean visual acuity increased from 0.9±1.1 (0-3.1) logMAR before treatment to 0.59±1.1 (0-3.1) logMAR after treatment (p=0.006). Post-treatment visual acuity reached 0.2 logMAR or better in 15 patients (15/21, 71.4%; visual acuity could not be measured in one child).

Discussion

CL use is one of the known risk factors for the development of MK.[10] The prevalence of these infections, which may require long-term treatment, is increasing as the use of CLs becomes more widespread.[6,11] Determining whether keratitis in a CL user is secondary to a microbial infection is very important in determining the follow-up and treatment approach. MK is mainly a clinical diagnosis, and the inability to demonstrate the causative pathogen by microbial analyses does not rule out an infectious etiology.[4] However, identifying the causative pathogen is necessary to support the clinical diagnosis and determine antimicrobial therapy.[12] In the literature, pathogens are identified by microbiological tests at rates of 50-80%.[3] This rate was 68.1% in our study, within the range reported in the literature.

In addition to the corneal samples obtained from patients with CL-related MK, microbial examinations of samples taken from the CL itself and the lens case and solution should also be

performed. Samples from CL-related materials have advantages such as being unaffected by the topical anesthetics used and sampling errors during corneal scraping.[6] Although high rates of bacterial contamination in the lens cases of asymptomatic users may suggest the risk of false positivity, these samples remain important in investigations to determine keratitis pathogens.[4,13] In our study, CL-related material from only 5 patients (22.7%) could be obtained for microbial examination. In another study examining CL-related MK cases in our country, the lens cases and solutions of only 19% of the patients were available.[3] These results suggest that CL users in Turkey are not adequately informed about this issue. In this respect, it is important to inform CL users that they should bring their CL-related materials with them when presenting to a physician because of a symptom.

In their study of 43 CL-related MK cases, Chaudhry et al.[2] reported that 88.3% of the patients were female and that most of these patients (61.5%) used cosmetic CLs. A high female to male ratio among CL-related MK patients has also been reported in other studies.[3,14] Unlike in the study by Chaudhry et al.[2], the rate of cosmetic CL use was quite low in our study, but the proportion of female patients was quite high (16/22, 72.7%). In addition, most of the female patients (13/16, 81.2%) were under 35 years of age. These data should not be interpreted as female gender being a risk factor for CL-related MK. On the contrary, there are studies in the literature reporting that male gender is a risk factor for these infections.[11,15] The female predominance in CL-related MC may be due to the fact that CL use is more common among women in our society.

Seasonal characteristics are known to be associated with CL-related MK.[16] Green et al.[17] reported that 62.3% of the cases presented between December and April in their study examining CL-related MK cases over a 16-year period. Hoddenbach et al.[4] reported that the highest number of cases in their series presented during the summer. The authors noted that hot and humid conditions facilitate infection and also suggested more frequent swimming and greater risk of sleeping with CLs in increased travel in the summer months as possible reasons.[4] In our study, most patients presented in autumn and winter. This seasonal distribution of our cases is consistent with the results of Morgan et al.[18], who reported that the risk of developing corneal infiltrates in CL users was 2-4 times higher in winter than in summer. The authors attributed this finding to seasonal variability in the systemic health status of patients and stated that the lower incidence of corneal infiltrative events in patients without systemic health problems supported their results.

Many risk factors for CL-related MK have been identified. Improper CL use, maintenance, and cleaning, overnight wear regimens/schedules, being a new CL user, smoking, and DM are the leading factors.[1,2,10,19] In our study, 4 patients were smokers, only 1 patient had DM, and no chronic ocular surface disease was detected in any of the patients. In addition, an overnight CL wear regimen was only recommended for a pediatric patient. However, mistakes in CL use and care were detected in the majority of our patients. A history of sleeping with CLs was the most common risk factor, noted in 15 cases (68.1%). Similarly, Palamar et al.[6] reported sleeping with CLs at night and swimming in the pool and sea with CLs at rates of 63.6% and 27.2%, respectively, in their CL-related MK patients. Different studies have shown the importance of adequately informing CL users about lens use and care in preventing CL-associated infections.[20,21] The above-mentioned results reported from Turkey support the literature in this sense and show that the care required in this matter remains important in our country.

In our study, similar to the literature, gram-negative pathogens (78.2%) constituted the majority of the isolated bacterial agents.[3,5,10] *P. aeruginosa* was reported as the most commonly isolated agent in CL-associated MK cases in several studies, and was also the most commonly detected pathogen in our series (n=8).[10,11,22] These bacteria attach to the CL surface by forming a biofilm layer that increases their resistance to the antimicrobial defense mechanisms of the tears and corneal epithelium.[1] Reduced tear exchange under the CL and additional virulence factors of the pathogens (e.g., adhesins, various toxins) also facilitate the development of corneal infection.[1] Combined fortified vancomycin-amikacin is one of the leading options in empirical therapy for MK.[23,24] In cases of CL-related MK, ceftazidime is another option that can be used against gram-negative pathogens, as *Pseudomonas* spp. are among the most frequently detected agents.[6] Moxifloxacin monotherapy can also be preferred for empirical treatment in patients with milder clinical signs.[24,25] The antibiotic susceptibility results of the bacterial agents detected in our patients showed that all of the abovementioned antibiotic options were largely effective against the active microorganisms. Susceptibility rates among the causative pathogens were 84.2% for combined vancomycin-amikacin, 95% for combined vancomycin-ceftazidime, and 94.7% for moxifloxacin (Table 3). This result supports the validity of the empirical antibiotic options preferred in the classical approach.

In CL-related MK, the infection may progress and require keratoplasty despite aggressive medical treatment.[5] In the literature, the need for keratoplasty has been reported as 5-20% in these cases.[4,5,14] In our study, recovery was achieved with medical treatment in 17 patients, while 2 patients (10.5%) underwent tectonic keratoplasty, a result within the range reported in the literature in terms of anatomic success. The mean visual acuity of our patients at first admission was 0.9 logMAR, similar to the averages reported in the literature (0.5-2 logMAR range).[3,5,6,10,26] Sharma et al.[26] reported that among patients with MK associated with soft CL use who presented with relatively worse initial visual acuity than our patients, 53.3% had a visual acuity of 0.2 logMAR or greater (≥20/30 in the relevant study). In a study of CL-related MK cases of bacterial etiology that presented in 2004-2005 and had similar pre-treatment visual acuity to our patient group, Yu et al.[10] reported that 57% had a post-treatment visual acuity of 0.2 logMAR or greater. In our study, post-treatment visual acuity of 0.2 logMAR and above

was achieved in 15 patients (15/21, 71.4%; visual acuity could not be measured in one child). The visual outcomes in our series were quite satisfactory considering their visual acuity at admission.

Our clinic is in a tertiary reference center and many patients received various antimicrobial treatments before they were referred to us. Therefore, it is possible that our study demonstrates the outcomes of relatively resistant cases rather than a general CL-related MK case profile. The retrospective design can be considered another limitation of our study.

Conclusion

CL-associated MK is a serious infection that can result in permanent vision loss. In a large proportion of patients, mistakes related to CL use and/or cleaning are a facilitating factor. Informing CL users in detail about CL use and cleaning may reduce the frequency of these mistakes and thus infections. CL users must also be made aware that they should bring CL-related materials with them when consulting a physician for ocular symptoms. Gram-negative bacteria, especially *P. aeruginosa,* are the most common pathogens involved in these infections. The current antibiotic options that should be preferred in empirical treatment continue to be effective against likely pathogens. With a thorough diagnostic work-up and appropriate treatment approaches, successful visual outcomes can be achieved in most cases.

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Ethics

Ethics Committee Approval: Approval for the study was obtained from the Çukurova University Faculty of Medicine Ethics Committee (decision number: 19, meeting number and date: 108/12.02.2021) and the study was conducted in accordance with the principles of the Declaration of Helsinki.

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.Y., E.E., İ.İ.H., Concept: M.Y., İ.İ.H., E.E., Design: İ.İ.H., E.E., M.Y., Data Collection or Processing: D.Ç., F.K., İ.İ.H., Analysis or Interpretation: İ.İ.H., E.E., M.Y., F.K., Literature Search: İ.İ.H., D.Ç., E.E., Writing: İ.İ.H., E.E., M.Y., F.K., D.Ç.

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References

1. Zimmerman AB, Nixon AD, Rueff EM. Contact lens associated microbial keratitis: practical considerations for the optometrist. Clin Optom (Auckl). 2016;8:1-12.
2. Chaudhry TA, Sarfraz S, Khan Q, Ahmad K. Contact lens-related visual loss-a case series from Karachi. J Pak Med Assoc. 2011;61:1246-1248.
3. Karaca I, Barut Selver O, Palamar M, Egrilmez S, Aydemir S, Yagci A. Contact Lens-Associated Microbial Keratitis in a Tertiary Eye Care Center in Turkey. Eye Contact Lens. 2020;46:110-115.
4. Hoddenbach JG, Boekhoorn SS, Wubbels R, Vreugdenhil W, Van Rooij J, Geerards AJ. Clinical presentation and morbidity of contact lens-associated microbial keratitis: a retrospective study. Graefes Arch Clin Exp Ophthalmol. 2014;252:299-306.
5. Saeed A, D'Arcy F, Stack J, Collum LM, Power W, Beatty S. Risk factors, microbiological findings, and clinical outcomes in cases of microbial keratitis admitted to a tertiary referral center in ireland. Cornea. 2009;28:285-292.
6. Palamar M, Masaroğulları M, Eğrilmez S, Aydemir Ş, Yağcı A. Our Microbiological Analysis Results in Microbial Contact Lens Keratitis. Turk J Ophthalmol. 2010;40:349-343.
7. Stapleton F, Edwards K, Keay L, Naduvilath T, Dart JK, Brian G, Holden B. Risk factors for moderate and severe microbial keratitis in daily wear contact lens users. Ophthalmology. 2012;119:1516-1521.
8. Harbiyeli II, Oruz O, Erdem E, Cam B, Demirkazik M, Acikalin A, Kibar F, Ilkit M, Yarkin F, Yagmur M. Clinical aspects and prognosis of polymicrobial keratitis caused by different microbial combinations: a retrospective comparative case study. Int Ophthalmol. 2021;41:3849-3860.
9. IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.
10. Yu DK, Ng AS, Lau WW, Wong CC, Chan CW. Recent pattern of contact lens-related keratitis in Hong Kong. Eye Contact Lens. 2007;33:284-287.
11. Poggio EC, Glynn RJ, Schein OD, Seddon JM, Shannon MJ, Scardino VA, Kenyon KR. The incidence of ulcerative keratitis among users of daily-wear and extended-wear soft contact lenses. N Engl J Med. 1989;321:779-783.
12. Yalçın E, Karel F, Karaarslan A, Tekeli A. Kornea enfeksiyonlarının tanısında direkt yayma, kültür ve antibiyogramın önemi. MN Oftalmoloji. 1998;5:42-46.
13. Szczotka-Flynn LB, Pearlman E, Ghannoum M. Microbial contamination of contact lenses, lens care solutions, and their accessories: a literature review. Eye Contact Lens. 2010;36:116-129.
14. Verhelst D, Koppen C, Van Looveren J, Meheus A, Tassignon MJ; Belgian Keratitis Study Group. Contact lens-related corneal ulcers requiring hospitalization: a 7-year retrospective study in Belgium. Acta Ophthalmol Scand. 2006;84:522-526.
15. Stapleton F, Dart JK, Minassian D. Risk factors with contact lens related suppurative keratitis. CLAO J. 1993;19:204-210.
16. Stapleton F, Keay LJ, Sanfilippo PG, Katiyar S, Edwards KP, Naduvilath T. Relationship between climate, disease severity, and causative organism for contact lens-associated microbial keratitis in Australia. Am J Ophthalmol. 2007;144:690-698.

17. Green M, Sara S, Hughes I, Apel A, Stapleton F. Trends in contact lens microbial keratitis 1999 to 2015: a retrospective clinical review. Clin Exp Ophthalmol. 2019;47:726-732.
18. Morgan PB, Efron N, Brennan NA, Hill EA, Raynor MK, Tullo AB. Risk factors for the development of corneal infiltrative events associated with contact lens wear. Invest Ophthalmol Vis Sci. 2005;46:3136-3143.
19. Stapleton F, Keay L, Edwards K, Naduvilath T, Dart JK, Brian G, Holden BA. The incidence of contact lens-related microbial keratitis in Australia. Ophthalmology. 2008;115:1655-1662.
20. Hickson-Curran S, Chalmers RL, Riley C. Patient attitudes and behavior regarding hygiene and replacement of soft contact lenses and storage cases. Cont Lens Anterior Eye. 2011;34:207-215.
21. McMonnies CW. Improving patient education and attitudes toward compliance with instructions for contact lens use. Cont Lens Anterior Eye. 2011;34:241-248.
22. Lam DS, Houang E, Fan DS, Lyon D, Seal D, Wong E; Hong Kong Microbial Keratitis Study Group. Incidence and risk factors for microbial keratitis in Hong Kong: comparison with Europe and North America. Eye (Lond). 2002;16:608-618.
23. Chiang CC, Lin JM, Chen WL, Chiu YT, Tsai YY. Comparison of topical fixed-combination fortified vancomycin-amikacin (VA solution) to conventional separate therapy in the treatment of bacterial corneal ulcer. Eye (Lond). 2009;23:294-298.
24. https://todakademisi.com/rehberler/13/bakteriyel-keratitler-tani-ve-tedavi-rehberi. Erişim tarihi: 10.1.2021.
25. Austin A, Lietman T, Rose-Nussbaumer J. Update on the Management of Infectious Keratitis. Ophthalmology. 2017;124:1678-1689.
26. Sharma S, Gopalakrishnan S, Aasuri MK, Garg P, Rao GN. Trends in contact lens-associated microbial keratitis in Southern India. Ophthalmology. 2003;110:138-143.