Epidemiology of bacterial corneal ulcers at tertiary centres in Vancouver, B.C.

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ABSTRACT ●

Objective: To report the epidemiology of culture-positive bacterial corneal ulcers in Vancouver, B.C., Canada.

Design: Retrospective, observational case series.

Methods: Predetermined search terms were entered into the hospitals' electronic microbiology databases to create a cohort of patients who had undergone corneal scrapings for ulcers from April 2006 to March 2011. All specimens were plated on culture media. Cultured species were identified, and antimicrobial sensitivities were obtained. Clinical charts were then reviewed to identify associated risk factors.

Results: In total 281 corneal scrapings were included, with a positive culture recovery rate of 75%. Bacterial keratitis accounted for 84.8% of culture-positive ulcers, followed by fungi (10%) and finally *Acanthamoeba* (5.2%); 73% of ulcers were monomicrobial in origin and 28% polymicrobial. We found an increase in Gram-negative micro-organisms over time. General sensitivity to antibiotics did not change over time. A major risk factor for Gram-positive involvement was ocular surface disease, whereas contact lens wear was a major risk factor for Gram-negative involvement.

Conclusions: Bacterial keratitis was found to be the major cause of infectious keratitis in Vancouver, B.C. The majority of bacterial ulcers were caused by Gram-positive bacteria. However, we found an increase in Gram-negative involvement over time. Contact lens wear was identified as the major risk factor for development of Gram-negative ulcers. Pre-existing ocular disease was associated with Gram-positive infection. Susceptibility of Gram-negative bacteria to common broad-spectrum antibiotics was high, but susceptibility of Gram-positive bacteria to these antibiotics was lower and more variable.

Microbial keratitis is an important cause of ocular morbidity and can result in significant visual loss. Empiric therapy is therefore often initiated before culture results are available. Furthermore, smaller noncentral ulcers are often treated without corneal scrapings. Empiric antibiotic therapy should be broad enough to cover the most frequent and serious pathogens. Because bacterial prevalence and sensitivity patterns vary by region and over time, local epidemiologic surveys are necessary to develop up-to-date treatment guidelines for microbial keratitis. In addition, latest ocular surveillance data on antibiotic resistance trends show increased levels of resistance among multiple pathogens, emphasizing the need for ongoing surveillance studies.[1–3] Recently the first Canadian surveillance study, an extension of the Antibiotic Resistance Monitoring in Ocular micRorganisms (ARMOR) study, showed high resistance levels among *Staphylococci* (unpublished data).[4]

In this study, we reviewed the microbiology of infectious corneal ulcers at tertiary centres in Vancouver, B.C., over a period of 5 years. Our goals were, first, to determine the prevalence of causative agents of infectious keratitis; second, to study their susceptibility patterns; and, third, to report any trends over the 5 years. Finally we also studied risk factors for development of bacterial corneal ulcers, especially any association with contact lens wear.

Patients and Methods

Our study conformed to the tenets of the Declaration of Helsinki and was approved by the UBC Clinical Research Ethics Board. All patients who underwent a corneal scraping and culture for suspected microbial keratitis between April 2006 to March 2011 were included in the study. We divided the timeframe in 2 periods for analysis of trends: 2006–2008 and 2009–2011.

Specimens were obtained after corneal scraping and routinely inoculated onto tryptic soy agar containing 5% sheep red blood cells, chocolate agar, and Sabouraud agar plates and into thioglycolate broth. In the case of a suggestive clinical picture, selective media were used to detect anaerobic bacteria, *Acanthamoeba* and *Mycobacteria*. Specimens were analysed by Medical Microbiology Laboratory at Vancouver General Hospital. Organisms were identified by reference methods.[5] In vitro sensitivity to different antibiotics was determined for each group of bacteria. The selection of the different antibiotics tested

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was determined according to the detected organism and the local protocol.

Clinical charts were then reviewed for associated risk factors, such as contact lens wear, ocular surface disease (blepharitis, neurotrophic keratopathy, tear-film deficiencies, etc.), previous ocular or eyelid surgery, systemic illness (immunosuppression, diabetes mellitus, graft-versus-host disease, atopic dermatitis, etc.), and corneal trauma.

Chi-square and Fisher exact tests were used for statistical analysis of the categorical variables. All calculations were performed using SPSS 20.0 software (SPSS Inc, Chicago, IL). A p-value of <0.05 was regarded as statistically significant.

Results

Over the 5-year time frame, a total of 281 corneal scrapings were performed in 280 patients (153 from 2006 to 2008 and 128 from 2009 to 2011). The mean age of the study group was 57.0 ± 19.5 years, with a 1:1 male/female and right eye/left eye proportion. The positive culture recovery rate was 75% in both periods (115/153 and 96/128 positive cultures in the first and second study period, respectively). Overall 131 out of 281 scrapings (46.6%) had antibiotic pretreatment (48.4% [74 of 153] in the first study period; 44.5% [57 of 128] in the second study period) ($p = 0.52$). Approximately 27% of the culture-positive scrapings were polymicrobial in both study periods. In non-contact lens–related polymicrobial ulcers over the whole study period, 100% of the infections involved Gram-positive bacteria, 27.7% Gram-negative bacteria, and 4.3% fungi. Contact lens–related polymicrobial ulcers, on the other hand, showed 72.7% Gram-positive involvement, 9.1% Gram-negative involvement, 9.1% fungal involvement, and 9.1% involvement of *Acanthamoeba*. Bacterial keratitis accounted for 84.8% of culture-positive ulcers, followed by fungal (10%) and *Acanthamoeba* (5.2%). Table 1 illustrates the range of cultured bacteria by Gram staining group per period. The total number of Gram-positive and Gram-negative isolates was 115 (86%) and 19 (14%), respectively, in the first study period, and 85 (72%) and 33 (28%), respectively, in the second study period. This increased proportional involvement of Gram-negative over Gram-positive organisms was statistically significant ($p = 0.008$). The most frequent cultured organism was coagulase-negative *Staphylococcus* (CNS) (72 isolates or 28.6% of all bacterial recovery), and thus it was also the most common Gram-positive bacteria, accounting for 36% of the Gram-positive isolates. Out of 72 CNS isolates, 27 were monomicrobial (37.5%). Of all the CNS growth results, one was reported as "probable plate contaminant." This was from a monomicrobial isolate. There was no other record in the database of any "scant growth." The most common Gram-negative bacteria were *Moraxella* species (17 isolates or 6.7% of all bacterial growth), accounting for 32.7% of the Gram-negative recovery. The only significant change in prevalence of specific organisms over time was the decreased involvement of *Staphylococcus aureus* in the second study period ($p = 0.02$).

Table 1—Most frequent cultured bacteria by Gram group per period

Bacterial Isolates	2006–2008, N (% of Bacterial Isolates)	2009–2011, N (% of Bacterial Isolates)	p
Gram-positive isolates	115 (85.8)	85 (72.0)	0.008*
Staphylococcus aureus	25 (18.7)	9 (7.6)	0.015*
MRSA	3 (2.2)	2 (1.7)	1.000
CNS	36 (26.9)	36 (30.5)	0.577
MRCNS	4 (3.0)	3 (2.5)	1.000
Streptococcus species	19 (14.2)	16 (13.6)	1.000
Corynebacterium species	13 (9.7)	8 (6.8)	0.496
Other	15 (11.2)	11 (9.3)	0.682
Gram-negative isolates	19 (14.2)	33 (28.0)	0.008*
Pseudomonas species	4 (3.0)	9 (7.6)	0.152
Moraxella species	7 (5.2)	10 (8.5)	0.326
Serratia species	3 (2.2)	5 (4.2)	0.480
Haemophilus influenzae	1 (0.7)	4 (3.4)	0.189
Other	4 (3.0)	5 (4.2)	0.738

CNS, coagulase-negative *Staphylococcus*; MRCNS, methicillin-resistant coagulase-negative *Staphylococcus*; MRSA, methicillin-resistant *Staphylococcus aureus*.

*$p < 0.05$.

Association with contact lens wear was encountered in 20.8% (24/115) and 19.8% (19/96) of culture-positive cases in both study periods, respectively. Contact lens–related ulcers were mainly caused by bacteria (67.4%), followed by parasites (20.9%) and fungi (11.6%). Table 2 illustrates the range of cultured bacteria by Gram group per period for contact lens–related ulcers. The total number of Gram-positive and Gram-negative isolates was 11 (78.6%) and 3 (21.4%), respectively, in the first study period, and 9 (60%) and 6 (40%), respectively, in

Table 2—Most frequent cultured bacteria in contact lens–related ulcers by Gram group per period

Bacterial Isolates in CL-Related Ulcers	2006–2008, N (% of CL-Related Bacterial Isolates)	2009–2011, N (% of CL-Related Bacterial Isolates)	p
Gram-positive isolates	11 (78.6)	9 (60.0)	0.427
Staphylococcus aureus	0 (0.0)	1 (6.7)	1.000
CNS	6 (42.9)	5 (33.3)	0.710
Streptococcus species	1 (7.1)	3 (20.0)	0.598
Corynebacterium species	1 (7.1)	0 (0.0)	0.483
Other	3 (21.4)	0 (0.0)	0.100
Gram-negative isolates	3 (21.4)	6 (40.0)	0.427
Pseudomonas species	2 (14.3)	4 (26.7)	0.651
Moraxella species	0 (0.0)	1 (6.7)	1.000
Serratia species	1 (7.1)	1 (6.7)	1.000
Haemophilus influenzae	0 (0.0)	0 (0.0)	1.000

CL, contact lens; CNS, coagulase-negative *Staphylococcus*.