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# Clinical and microbiological profile of infectious keratitis in an area of Madrid, Spain

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ABSTRACT

*Introduction:* To study antibiotic susceptibility in bacterial keratitis (BK), its profile over 10 years and its influence on ophthalmological practice.
*Methods:* Retrospective review of BK with positive corneal scraping over a 10-year period. Risk factors for keratitis, visual acuity (VA), empirical topical treatment, corneal infection characteristics and outcomes were analyzed for BK due to *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus pneumoniae*, *Pseudomonas aeruginosa* and *Propionibacterium acnes*.
*Results:* 389 positive corneal scrapings were collected. All Gram-positive bacteria were susceptible to vancomycin. *P. aeruginosa* demonstrated >90% sensitivity to the most-commonly-used topical antibiotics. Susceptibility to methicillin was 90.2% for *S. aureus* and 66.3% for *S. epidermidis*. The results of 215 patients were available. 1.9% required enucleation and 2.8% required surgical treatments. Final VA improved after treatment in keratitis due to *S. aureus* ($p = 0.026$) and *S. epidermidis* ($p = 0.005$). There was a correlation between *S. aureus* resistance to methicillin ($p = 0.002$) and levofloxacin ($p = 0.043$) and enucleation (20% and 10%, respectively) compared with a 0% rate of enucleation in *S. aureus*-susceptible keratitis.
*Conclusions:* BK due to *S. pneumoniae* is very aggressive irrespective of antibiotic sensitivity. *S. aureus* was frequently isolated in patients with systemic diseases. It causes severe keratitis and remains moderately resistant to methicillin and levofloxacin. For this reason, keeping vancomycin in empirical regimens is believed to be necessary.



## Perfil clínico y microbiológico de la queratitis infecciosa en un área de Madrid, España

*Palabras clave:*
Susceptibilidad a antibióticos
Queratitis bacteriana
Infecciones corneales
Queratitis
Enucleación

RESUMEN

*Introducción:* Estudiar la susceptibilidad antibiótica en queratitis bacteriana (QB), el perfil temporal a lo largo de 10 años y su influencia en la clínica ocular.
*Métodos:* Revisión retrospectiva durante un periodo de 10 años de QB con raspado corneal positivo. Se analizaron los factores de riesgo de queratitis, la agudeza visual (AV), el tratamiento empírico tópico, las características de la infección corneal y el resultado clínico para QB por *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus pneumoniae*, *Pseudomonas aeruginosa* y *Propionibacterium acnes*.
*Resultados:* Se recogieron 389 raspados corneales positivos. Todas las bacterias grampositivas fueron susceptibles a la vancomicina. *P. aeruginosa* presentó sensibilidad mayor del 90% a los antibióticos tópicos más comúnmente utilizados. La susceptibilidad a la meticilina fue del 90,2% para *S. aureus* y del 66,3% para *S. epidermidis*. Los resultados clínicos estaban disponibles para 215 pacientes. El 1,9% requirieron

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enucleación y el 2,8% tratamientos quirúrgicos. La AV final mejoró después del tratamiento en queratitis por *S. aureus* (p = 0,026) y por *S. epidermidis* (p = 0,005). Hubo correlación entre la resistencia de *S. aureus* a la meticilina (p = 0,002) y levofloxacino (p = 0,043) y enucleación (20 y 10%, respectivamente) en comparación con una tasa de enucleación del 0% en *S. aureus* susceptible.
*Conclusiones:* Las QB por *S. pneumoniae* son muy agresivas independientemente de la sensibilidad antibiótica. *S. aureus* se aisló con frecuencia en pacientes con enfermedades sistémicas, causa queratitis severa y permanece moderadamente resistente a la meticilina y a levofloxacino; debido a esto, consideramos necesario mantener la vancomicina en la pauta empírica.


## Introduction

Bacterial infectious keratitis (BK) is a common reason of consulting in ophthalmology and is associated with high morbidity. All cases of moderate to severe keratitis require a detailed laboratory work-up, which ensures that if there is partial or no response to initial therapy, the antimicrobial treatment can be modified based on the results of culture and susceptibility tests. Generally, broad-spectrum antibiotics are used as empiric first-line treatment for presumed BK after obtaining appropriate corneal scrapes. The drugs chosen as initial therapy are either commercially available quinolone or a combination of fortified antibiotics, topical solutions prepared from parenteral antibiotics by reconstituting them with sterile injection water[1] or Balanced Salt Solution (BSS)[2] with one agent largely directed against Gram-positive and the other against Gram-negative organisms.

The maintenance of the effectiveness of the empiric therapy requires a low resistance rate of the bacteria that can cause keratitis. Longitudinal epidemiologic studies provide clinicians with vital information on the changing microbiological pattern of keratitis in their specific area concerning causative organisms and their antibiotic sensitivities,[3–5] which is critical for choosing the most suitable empirical regimen. These descriptive studies are gaining importance because monotherapy quinolone is currently being proposed as the main empirical option for bacterial keratitis although caution seems advisable when using monotherapy for any serious bacterial corneal ulcer.[6]

The main purpose of this study is to know the causative bacteria of corneal infection in our area, and their susceptibility profile. Secondary purpose are to analyze the temporal profile of the antibiotic susceptibility to the most relevant topical antibacterial agents, to describe the clinical presentation of the most frequent bacterial keratitis groups and to study if antibiotic resistance has any association with the clinical outcome. Significant trends in these factors over the 10 years of the study were sought to help to select the most convenient empiric initial regimen for BK in our area.

## Methods

A retrospective audit was performed of the isolate records of different episodes of patients with symptoms and biomicroscopic signs of BK who had a positive corneal scrape from January 2006 to December 2015 at a tertiary Hospital in Madrid, Spain. All the corneal smears and cultures were typically indicated in our hospital in cases of corneal infiltrates with at least one of the following criteria: dense infiltrate, epithelial ulcer of central location, association with anterior chamber cells 1+ (10 cells or greater in a 1-mm beam), absence or partial response to broad spectrum antibiotic therapy and or any infiltrate with clinical features suggestive of fungal, amoebic or mycobacterial keratitis. As well, samples were obtained usually in case of infiltrates or epithelial ulcers in relation with contact lens (CL) users.

Specimens were collected in the cornea unit, emergency room or surgery room by corneal scraping procedure and direct inoculation onto the appropriate culture media by the 24 h on call microbiologist at any day or night time. Gram stains were immediately performed on smears, whereas blood, chocolate blood agar plate with hemin and vitamin K1 and Sabouraud agar plates were inoculated. Incubation time for plates varied between 7 and 10 days from blood and chocolate agar plates, and up to 4 weeks for Sabouraud agar plates. Blood and chocolate agar plates were incubated in carbon dioxide environments at 35 °C, whereas two Sabouraud agar plates were incubated in oxygen environments at 25 °C and 35 °C. A second blood agar plate with hemin and vitamin K1 was incubated in an anaerobic environment at 35 °C for 14 days.

To exclude accidental contaminants, the minimum criterion for a positive culture was the growth of at least 3 colonies on one solid medium with similar morphology to the Gram stain, if this was positive. Cultures that isolated multiple organisms were analyzed separately. Antibiotic resistance was determined by broth microdilution to determinate the Minimum Inhibitory Concentrations. The antibiotics tested for the isolated microorganisms are described in Table 1. The interpretations for sensitive, intermediate and resistant were in accordance with EUCAST 4.02014 standards.[7]

Risk factors for keratitis, initial and final visual acuity (VA) (final VA was the VA on the last visit before medical discharge for the episode), topical empirical treatment, characteristics of the corneal infection and clinical outcome were analyzed from patients with a positive corneal scrape for *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus pneumoniae*, *Pseudomonas aeruginosa* and *Propionibacterium acnes* keratitis. Influence of antibiotic susceptibility to clinical outcome (enucleation, corneal surgery and number of days of antibiotic treatment) was analyzed.

The statistical analysis was performed using SPSS 11.5.[8] Causative bacteria of keratitis and their susceptibility profile were described with their relative frequency and counts. Lineal by lineal association test was used to analyze the temporal profile of the antibiotic susceptibility to the most relevant topical antibacterial agents between 3 periods, over the 10 years of the study. For the description of the keratitis episodes clinical data, quantitative variables were described with their mean and the standard deviation (SD) and the days of treatment variable with median and interquartile range. The qualitative variables were described with their relative frequency and counts. Finally, to study if antibiotic resistance has any effect in the clinical outcome, a comparative statistical analysis has been done: the Fisher Test was used in $2 \times 2$ cross tables, in any other case Chi-square was considered. For quantitative variable (days of treatment) Mann–Whitney test was used. To compare the two related samples of visual acuity (VA), the Wilcoxon Test was used.

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