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Practice patterns in the management of bacterial keratitis: a five-continent survey

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Abstract

Purpose To assess the current diagnostic and therapeutic practice patterns in early management of bacterial keratitis over five continents.

Methods Between March and August 2019, we distributed an online survey including two clinical scenarios of bacterial keratitis, namely, a mild case and severe case, to 2936 ophthalmologists from 144 countries around the world. The survey consisted of 29 questions. We performed descriptive statistics and a comparative analysis of the answers according to the participants' continent of practice, practice setting, seniority, and subspecialty.

Results We received 237 surveys from 54 countries (8% response rate). The proportion of respondents performing microbiological investigations was higher in North America, Asia, Europe, and Oceania than Africa and South America ($p<0.05$). This ratio was also higher among ocular surface specialists than for other ophthalmologists ($p<0.001$). For mild cases, fluoroquinolone monotherapy and a combination of two or more antibiotics were prescribed by 46% and 41% respondents, respectively. For severe cases, fluoroquinolone monotherapy and a combination of antibiotics were prescribed by 20% and 78% respondents, respectively. Fluoroquinolone monotherapy was the most commonly prescribed treatment in South America, Africa, and Oceania. A combination of two antibiotics was preferentially prescribed in the rest of the world. Topical steroids were prescribed in both circumstances, respectively, in 72% and 75% of cases.

Conclusion Our results highlight essential geographical disparities in the current management of bacterial keratitis over five continents.

Keywords Antibiotics · Bacterial keratitis · Diagnosis · Survey · Treatment

Key messages

What is known

- Bacterial keratitis is a common concern in ophthalmological emergencies, with no consensus among ophthalmologists regarding its diagnosis and treatment.

What is new

- Ophthalmologists from North America, Asia, Europe and Oceania are more likely to perform microbiological investigations than those from Africa and South America.
- Ocular surface specialists are more likely to perform corneal scrapping than other ophthalmologists.
- A combination of two antibiotics is the preferred treatment, but its nature is highly variable depending on the respondents' geographical location.

Survey of Management of Infectious Keratitis study group, members listed in the Appendix.

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Introduction

Bacterial keratitis (BK) is a common concern in ophthalmological emergencies, as it may lead to severe visual disability [1]. Infection severity usually depends on: (i) underlying condition of the cornea (i.e., host defenses and healing capacities); (ii) corneal location as well as the number and pathogenicity of infecting bacteria(s); and (iii) initial management and follow-up of the patient.

BK requires a standardized work-up procedure so as to avoid diagnostic and therapeutic delays that may negatively affect visual prognosis. Many patients display a poor clinical outcome if aggressive and appropriate therapy is not promptly initiated [2]. BK prognosis may also be influenced by geographic and climatic factors. Several differences have been noted between populations living in rural areas or cities and in northern countries or southern areas.

Despite the publication and diffusion of recommendations via scientific papers and textbooks, there seems to be no consensus yet among ophthalmologists around the world about BK diagnosis and therapeutic management. Many aspects of BK management remain controversial, such as the use of fortified antibiotics and topical steroids, as well as the criteria required for patient hospitalization [3, 4]. Moreover, microbiological epidemiology and access of medical doctors to continuing medical education, as well as accessibility to medical care and anti-infective treatments, significantly differ depending on the region of the world [5–7], thereby causing disparities in clinical practices.

This study sought to assess current clinical practice patterns in initial BK management over five continents.

Material and methods

This study was approved by the ethical committee of the French ophthalmological society (SFO) and conducted in accordance with the tenets of the Declaration of Helsinki. An online survey concerning the management of bacterial keratitis was proposed to ophthalmologists over five continents including Africa, America, Asia, Europe, and Oceania. A similar study regarding fungal keratitis and *Acanthamoeba* keratitis was conducted simultaneously by our group. Its results have been published previously [8].

Patients and public involvement

None.

Survey development

The survey was developed using Google Forms, a survey administration application that is included in the Google Drive office suite (Google, Mountain View, CA, USA), with a questionnaire submitted to each participant by email in either French or English. The first part of the questionnaire aimed to collect information about the participants, such as the geographical location of their practice (city, country), structure in which they practiced (hospital/general practice), their main subspecialty, and professional experience. An email address was required to avoid duplicate submission of the survey, whereas data collection and analysis were conducted anonymously. In the second part of the survey, two clinical cases of patients suffering from BK were introduced using a short text illustrated by a slit lamp photograph of the infected cornea. We selected both a mild case of BK characterized by a small peripheral infiltrate (Fig. 1) occurring in a patient suffering from blepharitis and a severe case with a large infiltrate within the visual axis accompanied by an anterior chamber reaction occurring in a contact lens wearer (Fig. 2). For each case, we knew with certainty the final microbiological diagnosis, which while not known by the participant, was hinted at in the short text. Closed or multiple-choice questions were then asked concerning the need for microbiological examination in each case, the nature and regimen of the local anti-infectious treatment, and the prescription of a systemic antibiotic, as well as the use of topical steroids and delay before their implementation. Additionally, we asked the respondents if they would manage the case either as an ambulatory or hospitalized patient. Open-ended questions allowed participants to specify a treatment not listed among the multiple-choice questions or to add additional comments.

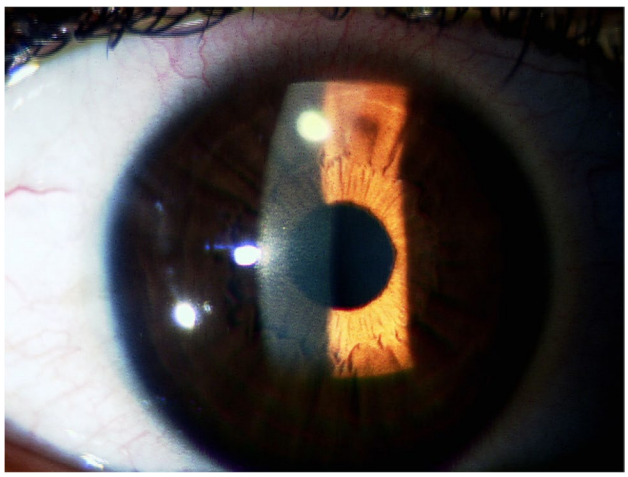

Fig. 1 First clinical case: mild bacterial keratitis. An 82-year-old man, with a history of chronic posterior blepharitis and dry eye disease, presents with redness and pain of the right eye for four days. The slit lamp examination highlights a small peripheral corneal ulcer without any anterior chamber inflammation. Gram-positive cocci keratitis is suspected

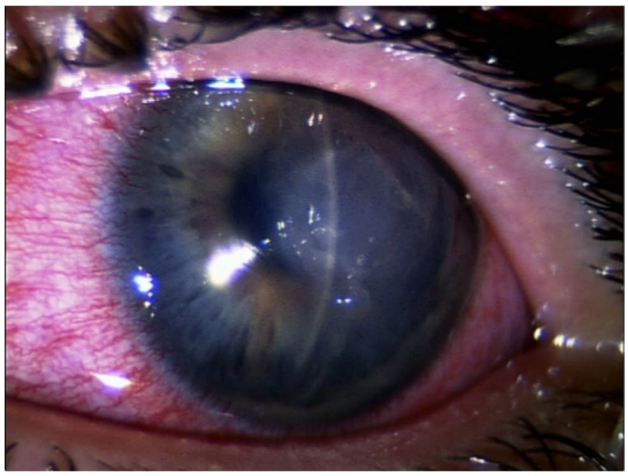

Fig. 2 Second clinical case: severe bacterial keratitis. A 32-year-old woman, with a history of monthly hydrophilic soft lens misuse (night-time wear and failure to meet renewal deadlines) presents with acute redness and pain of the left eye for 24 h. Visual acuity is limited to counting fingers. The slit lamp examination reveals a central infiltrate of 3 mm in diameter. There is an anterior chamber reaction 2+. Gram-negative rod keratitis is suspected

The 28 questions of the survey are available at the following URL: https://forms.gle/TJbKwENtASfMCUjZA (Supplemental digital content 1).

Diffusion of the survey

We sent a request for distribution to the 144 national ophthalmological societies listed with the International Council of Ophthalmology (ICO). We additionally contacted the national delegates of the European Board of Ophthalmology (EBO), as well as the French Ophthalmology Society (SFO) and their correspondents in foreign countries to identify ocular surface specialists in each country. We used the mailing list of the French College of University Ophthalmologists (COUF) to distribute our survey to French university hospitals. We also accessed PubMed® research using the keywords "cornea" and/or "keratitis" (as MeSH Major Topics) in each of the 197 countries of the world. We then collected the email addresses of the corresponding authors of each of the selected articles. We started to distribute the survey in March 2019 and sent a second message to each non-respondent 1 month after the first mailing. The diffusion of the survey ended in August 2019.

Statistical analysis

In the descriptive section, qualitative and quantitative variables collected were summarized in frequencies and percentages. For the crossover between several variables, the parametric Chi-square test was performed if the application condition enabled it. Otherwise, Fisher's exact test was applied. p values < 0.05 were selected as the threshold for statistical significance. We performed a comparative analysis according to the participants' geographical area of practice and type of structure in which they practiced, as well as their experience and subspecialty. We differentiated ocular surface subspecialties (i.e., corneal surgery, refractive surgery, contact lens adaptation, and eyelid surgery) from other ophthalmologists. Analyses were conducted using software R 3.1 Version (R Foundation for Statistical Computing, Vienna, Austria).

Results

The survey was sent to 2936 ophthalmologists from 144 countries, and we received 237 responses from 54 countries, representing an 8% response rate. Details of countries participating to the survey are listed in Supplemental digital content 2. Details regarding respondents' seniority, subspecialty, and practice setting can be found in Supplemental digital content 3.

The current diagnostic and therapeutic practice patterns for early BK management are summarized in Table 1.

Case of mild bacterial keratitis

The proportion of participants who carried out a microbiological diagnosis was significantly higher in North America (31%), Asia (38%), Europe (48%), and Oceania (29%) than in Africa (14%) and South America (5.3%), $p < 0.01$. This ratio was also higher among ocular surface specialists than other ophthalmologists (41% vs. 25%, respectively, $p = 0.015$). The examination was more frequently prescribed at hospitals than in general practice (41% vs. 18%, respectively, $p = 0.0013$). There was no difference when taking into account the respondents' seniority ($p = 0.83$).

Antibiotic prescriptions are detailed in Table 2. There were no significant prescription differences based on continent, subspecialty, practice setting, and seniority.

Systemic treatment was more often prescribed in general practice than at hospitals (15% and 6.1%, respectively, $p = 0.05$), whereas there were no significant prescribing differences when considering practice region, subspecialty, practice setting, and seniority.

In the event of a favorable post-antibiotic treatment outcome, 72.2% participants answered they would prescribe topical steroids (Fig. 3).

Case of severe bacterial keratitis

The proportion of participants performing microbiological investigations was statistically higher in North America

Table 1 Diagnostic and therapeutic practice patterns in the early management of bacterial keratitis (BK)

Clinical scenario		Mild BK	Severe BK
Microbial examination		35%	93%
Microbial sampling	Corneal scraping	90%	91.6%
	Conjunctival swab	23%	16.9%
	Contact lens analysis	NA	73.4%
	Contact lens case analysis	NA	57.4%
	Corneal biopsy	0%	0.8%
Microbiological analysis	Bacteriology	100%	93%
	Mycology	46%	68%
	Parasitology	13%	64%
	Virology	7%	14%
Management	Ambulatory	98%	53%
	Hospitalization	2%	47%
Antibiotics	Topical	See Table 2	See Table 3
	Systemic	8%	8%
Use of topical steroids		72%	75%

In the case of a mild and a severe BK, 35% and 93% of participants, respectively, answered that they would perform a microbiological examination. Patient management was carried out ambulatory in 98% mild BK cases and in 53% severe BK cases. For mild BK, 19 participants (8.2%) prescribed a systemic treatment with either tetracycline ($n=15$) or macrolide ($n=3$). For severe BK, a systemic therapy was prescribed in 8% of answers ($n=18$): fluoroquinolone ($n=5$), tetracycline ($n=4$), and antifungal ($n=3$). In the remaining cases ($n=4$), one or more additional antibiotics were used (cephalosporin, aminoglycoside, and/or vancomycin). *NA*, not applicable

Table 2 Topical antibiotic prescriptions for the treatment of mild bacterial keratitis: comparative analysis by practice region

Antibiotic prescription	Total $n=237$ (%)		Africa $n=44$ (%)		North America $n=13$ (%)		South America $n=19$ (%)		Asia $n=24$ (%)		Europe $n=130$ (%)		Oceania $n=7$ (%)	
Monotherapy	**139**	**(58.6)**	**25**	**(56.8)**	**11**	**(84.4)**	**17**	**(89.5)**	**18**	**(75)**	**62**	**(47.7)**	**6**	**(85.7)**
4th-generation quinolone	59	(24.9)	8	(18)	9	(69)	14	(73.7)	12	(50)	16	(12.3)	0	(0)
2nd- or 3rd-generation quinolone	50	(21.1)	6	(14)	0	(0)	3	(15.8)	3	(12.5)	34	(26.2)	4	(57.1)
Aminoglycoside	10	(4.2)	3	(6.9)	1	(7.7)	0	(0)	0	(0)	6	(4.6)	0	(0)
Chloramphenicol	9	(3.8)	6	(14)	0	(0)	0	(0)	0	(0)	2	(1.5)	1	(14.3)
Other antibiotic*	11	(4.6)	2	(4.5)	1	(7.7)	0	(0)	3	(12.5)	7	(5.4)	1	(14.3)
Dual therapy	**87**	**(36.7)**	**17**	**(38.7)**	**2**	**(14.4)**	**2**	**(10.5)**	**4**	**(16.7)**	**61**	**(46.9)**	**1**	**(14.3)**
Quinolone + aminoglycoside	22	(9.3)	4	(9.1)	0	(0)	0	(0)	0	(0)	18	(13.8)	0	(0)
Quinolone + chloramphenicol	14	(5.9)	5	(11.4)	0	(0)	0	(0)	0	(0)	4	(3.1)	1	(14.3)
Other association of antibiotics*	51	(21.5)	8	(18.2)	2	(23.1)	2	(10.5)	4	(16.7)	39	(30)	0	(0)
Three antibiotics or more*	**11**	**(4.6)**	**2**	**(4.5)**	**0**	**(0)**	**0**	**(0)**	**2**	**(8.3)**	**7**	**(5.4)**	**0**	**(0)**

Monotherapy and dual therapy were prescribed in 58.6% and 36.7% of cases, respectively. A combination of three or more antibiotics was prescribed by 4.6% of respondents. Among monotherapies, quinolone was prescribed in 46% of cases. Fourth-generation quinolones were more likely to be prescribed in North America (69%), South America (73.7%), and Asia (50%) than in Europe and Oceania, where quinolones of the second- and third-generations were more often prescribed (26.2%, and 57.1% respectively), yet without statistically significant differences ($p=0.28$). The treatment regimen was hourly in 27% cases, 8 to 10 times a day in 39% cases, and 4 to 6 times a day in 34% cases. *For all the other proposed antibiotics or combinations, the answers totaled < 5%. All entries regarding the number of antibiotics used is in boldface. All entries regarding the exact nature of the antibiotics used is not

(92%), Asia (92%), Europe (98%), and Oceania (100%) than in Africa (82%) and South America (84%), $p=0.0018$. This ratio was also statistically higher among ocular surface specialists than other ophthalmologists (97% vs. 86%, respectively, $p=0.0018$). There were no differences with respect to practice structure or respondents' seniority. Contact lens analysis was significantly more prescribed in Africa (69%), North America (75%), South America (69%), Asia (77%), and Europe (87%) than in Oceania (43%), $p=0.011$. Such analysis was also more often prescribed at hospitals than in

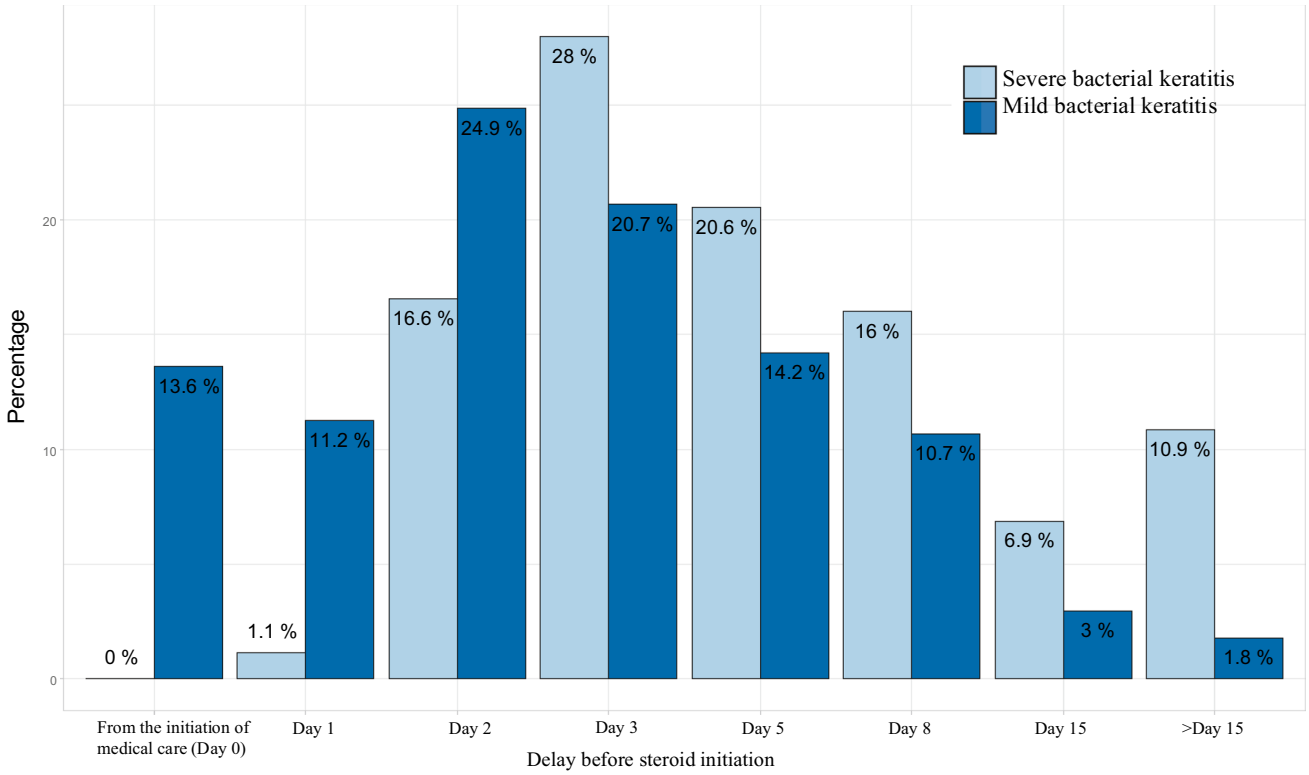

Fig. 3 Introduction of topical steroids after the beginning of the anti-infectious therapy. For the mild BK, 72.2% of participants prescribed local steroids. In 70.4% of cases, local steroids were initiated within the first 72 h following the beginning of the anti-infectious therapy. For the severe BK, 75% of participants prescribed local steroids. In 81.2% of cases, local steroids were introduced between 48 h and 8 days following the beginning of the anti-infectious therapy. There were no differences concerning the steroid prescription and delay before their initiation based on the respondents' practice region, specialty, seniority, and practice setting

general practices (85% vs. 63%, respectively, $p = 0.0021$). The same difference was observed for the analysis of contact lens cases and cleaning products (67% vs. 47%, respectively, $p = 0.018$). There were no differences with respect to the other sampling methods (i.e., corneal scraping and conjunctival swab), practice region, subspecialty, seniority, and practice setting.

Hospitalization was more often chosen in Africa (39%), Asia (50%), Europe (59%), and Oceania (86%) than in North America (8%) and South America (0%), $p < 0.001$. Hospitalization was more often considered necessary by practitioners working at hospitals than in a general practice setting (56% vs. 19%, respectively, $p < 0.001$). There were no difference depending on the respondents' subspecialty and seniority.

Detailed antibiotic prescriptions are listed in Table 3. Fourth-generation quinolone monotherapy was the most commonly prescribed treatment in South America (53%) and Africa (16%). Second- and third-generation therapies represented the main treatment in Oceania (43%). A combination of two fortified antibiotics was the preferred treatment in the rest of the world: vancomycin and aminoglycoside in North America (46%), first-generation cephalosporin and aminoglycoside in Asia (17%), and third-generation cephalosporin and vancomycin in Europe (15%). There were no significant differences in antibiotic prescriptions based on the respondents' subspecialty, seniority, and practice setting.

A systemic treatment was more often prescribed by ophthalmologists working in general practice than in hospitals (18% vs. 4%, respectively, $p = 0.0028$). There were no differences observed with respect to the respondents' practice region, subspecialty, or seniority.

In the event of a favorable outcome, 75% of participants prescribed topical steroids (Fig. 3).

Discussion

BK is an infectious emergency whose management is poorly codified worldwide. In this report, we have described the results of an international online survey among ophthalmologists regarding their microbiological work-up and therapeutic practice patterns for two clinical BK scenarios.

With 237 responses from 54 different countries, we were able to conduct an extended analysis across five continents. To our knowledge, only two studies with comparable goals and methodologies have previously been published, though

Table 3 Topical antibiotic prescriptions for the treatment of severe bacterial keratitis: comparative analysis by region of practice

Antibiotic prescription	Total $n=237$ (%)		Africa n=44 (%)		North America $n=13$ (%)		South America $n=19$ (%)		Asia $n=24$ (%)		Europe $n=130$ (%)		Oceania $n=7$ (%)	
Monotherapy	**52**	**(21.9)**	**12**	**(27.3)**	**2**	**(15.4)**	**11**	**(57.9)**	**4**	**(16.7)**	**19**	**(14.6)**	**4**	**(57.1)**
4th-generation quinolone	29	(12.2)	7	(15.9)	2	(15.4)	10	(52.6)	2	(8.3)	8	(6.2)	0	(0)
2nd- or 3rd-generation quinolone	19	(8)	4	(9.1)	0	(0)	1	(5.3)	1	(4.2)	10	(7.7)	3	(42.9)
Other antibiotic*	4	(1.7)	1	(2.3)	0	(0)	0	(0)	1	(4.2)	1	(0.8)	1	(14.3)
Dual therapy	**137**	**(57.8)**	**26**	**(59.1)**	**9**	**(69.2)**	**7**	**(36.8)**	**16**	**(66.7)**	**76**	**(58.5)**	**3**	**(42.9)**
Vancomycin + 3rd-generation cephalosporin	27	(11.4)	4	(9.1)	0	(0)	1	(5.3)	3	(12.5)	19	(14.6)	0	(0)
Vancomycin + aminoglycoside	16	(6.8)	0	(0)	6	(46.2)	1	(5.3)	0	(0)	9	(7)	0	(0)
Aminoglycoside + 1st-generation cephalosporin	15	(6.3)	5	(11.4)	0	(0)	1	(5.3)	4	(16.7)	4	(3.1)	1	(14.3)
Quinolone + aminoglycoside	23	(9.7)	7	(15.9)	1	(7.7)	1	(5.3)	2	(8.3)	12	(9.2)	0	(0)
Other combination*	56	(27)	10	(22.7)	2	(15.4)	3	(15.8)	7	(29.2)	32	(24.6)	2	(28.6)
Three antibiotics or more**	**48**	**(20.1)**	**6**	**(13.6)**	**2**	**(15.4)**	**1**	**(5.3)**	**4**	**(16.7)**	**35**	**(26.9)**	**0**	**(0)**

A monotherapy was prescribed in 21.9% cases and a combination therapy of two antibiotics in 57.8% cases. Three or more antibiotics were prescribed in 20.1% cases. The combinations were composed of two fortified antibiotics, a quinolone and a fortified antibiotic, or a quinolone and another commercially available antibiotic in 54%, 19%, and 27% cases, respectively. Hourly frequency of instillation was prescribed in 88% cases. Treatment was instilled 8 to 10 times a day in 9.7% cases and 4 to 6 times a day in 2.1% cases. *For all the other proposed antibiotics or combinations, the total of answers is < 5%. **The more commonly prescribed combination of three antibiotics, carboxypenicillin + aminoglycoside + vancomycin (5.9%), was only prescribed in France. For all the other combinations of three or more antibiotics, the answers totaled < 5%. All entries regarding the number of antibiotics used is in boldface. All entries regarding the exact nature of the antibiotics used is not

their diffusion was limited to the international members of the Cornea Society [9] and US members of the American Academy of Ophthalmology (AAO) [10]. The response rates were slightly superior to the 8% rate of our study, whereas our work covered a greater number of questions with a wider geographic diversity of respondents—European countries being the most widely represented—thus providing additional data. In contrast to previous studies, the questions about therapeutic management were open, enabling undirected and precise answers, while avoiding significant suggestion biases. In addition, we also compared the practices of ocular surface specialists with those of ophthalmologists from other subspecialties. This broad range of respondent seniority and practice settings allowed for a reflection on the relevance of the diagnostic examinations implemented, as well as the reasoned use of anti-infective drugs in a real-life context.

In the present survey, sampling was performed by 93% of the respondents for severe BK cases, using mostly corneal scraping or contact lens analysis. However, 35% participants chose to perform a microbiological examination for mild BK cases. Even if the majority of community-acquired BK cases resolve with empiric therapy and are managed without microbiological examination, the AAO, along with many textbooks, recommends performing a corneal scraping in cases of "central, large (> 2 mm), chronic corneal infiltrate with significant stromal thinning, not responding to broad spectrum antibiotic therapy, with a history of corneal surgery or atypical features that suggest acanthamoeba or fungal keratitis" [11, 12]. This recommendation clearly corresponds to the second case (severe BK) but not to the first (mild BK).

Therefore, the responses obtained by our survey reflect a very cautious attitude of ophthalmologists (namely, corneal specialists and those practicing in hospitals). In a number of cases, these ophthalmologists do not hesitate to extend microbiological work-up to all of the pathogens, including bacteria, amoebae, fungi, and viruses. This attitude may be related to the increasing prevalence of antibiotic resistances [13–15] and treatment failures, as well as to the respondents' own experience in BK management. Conversely, the proportion of microbiological samples in both cases was significantly lower in the developing countries of Africa and South America, possibly related to more difficult access to healthcare and trained microbiologists.

Interestingly, only 47% of respondents hospitalized severe BK cases, in spite of several severity criteria being present, such as large and central infiltrates. One explanation could be that healthcare facilities are often overcrowded in many countries, with the human resources needed to instill eye drops hourly at times being very limited [13]. The 2% hospitalization rate for mild BK cases is, however, in accordance with good practices, as recommended by the different societies and textbooks.

Although most textbooks and papers covering this topic recommend, in the absence of or before bacterial identification, fluoroquinolone monotherapy or a combination therapy of two fortified antibiotics that must cover both Gram-positive and Gram-negative bacteria, we observe that there is

no international consensus regarding the initial antibiotic therapy to be applied in BK. The results of the present study confirm the therapeutic management trends reported in previous surveys for severe BK cases. Thus, a combination of two fortified antibiotics is most commonly prescribed, namely, 57.8% in our study vs. 68% in Austin et al. [9], and 63% in Park et al. [10]. However, the nature of this combination was shown to be highly variable depending on the respondents' geographical location. The most commonly prescribed combination in our study was vancomycin and cephalosporin (11%), whereas Austin et al. reported cephalosporin and aminoglycoside as a first combination choice in 28% of answers and vancomycin and cephalosporin as a second choice (17%). These differences may be accounted for by a larger proportion of European (55%) and a lower number of US respondents (2%) in our study. A combination of three or more antibiotics was shown to be prescribed in 20% of severe cases. This is partly due to the observation that the triple regimen comprising carboxypenicillin and aminoglycoside and vancomycin proves to be widely used in France (37 respondents), without being reported in other countries. More generally, the number of combinations proposed by the respondents is further explained by the possibility of unguided answers offered by the Google questionnaire, as well as by national recommendations that are frequently made by a small number of experts in the ocular infection field.

Fluoroquinolone monotherapy was more commonly prescribed for mild BK (59%) than severe cases (22%), in line with the existing guidelines [3, 11]. The percentage of fourth-generation quinolone prescription was shown to be slightly higher compared with second- and third-generation quinolone (25% vs. 21% in the first case and 12% vs. 8% in the second), reflecting antibiotic availability across different markets. It is interesting to note that fourth-generation fluoroquinolones were available in 40, but not all of the 54, countries involved in this survey.

Several studies previously reported that fluoroquinolones and fortified antibiotics display equivalent efficacy [4], yet fluoroquinolones have a lower local toxicity and better patient compliance. In our survey, however, fortified antibiotics remain for many practitioners the first choice in cases of large or visually significant corneal infiltrates. Alternatively, combining quinolone + aminoglycoside appears rather popular, covering 37% of the prescriptions made for mild BK cases.

In addition, the heterogeneity of responses we received on the matter of sampling and initial choice of antibiotic therapy may be a consequence of regional variations in the etiology and resistance patterns of bacterial keratitis. This was well-described by Ung et al. in their recent review [16].

A large majority (72% and 75%) of respondents from all over the world use steroids to limit the BK-associated morbidity. Prescribing steroids was earlier limited to mild BK cases rather than severe ones. Using steroid eye drops for BK treatment theoretically leads to a decrease in the host's local inflammatory response, which causes corneal tissue destruction. However, there were controversies concerning the safety of steroids before the results of the "Steroids for Corneal Ulcers Trial" (SCUT) study were published. Although a review of the randomized trials available in the literature did not find any evidence concerning their effectiveness on visual acuity or corneal scar size [14], a long-term improvement in visual acuity in non-*Nocardia* severe BK has been reported [15]. An Australian case review revealed high-dose corticosteroids, such as six drops per day, to be significantly linked to better visual recovery [17]. Therefore, the core message of these essential publications has likely been followed by our survey respondents.

The international character of our study necessarily induces several weaknesses. First, there was unequal distribution of survey responses across the different countries. Due to the small number of respondents in some countries, the respective responses are unlikely to be representative of national practices. In addition, there are significant geographical disparities in risk factors, such as contact lens-related wear vs. traumatic keratitis cases, and in BK microbial epidemiology [5–7]; consequently, empiric treatment does not always target the same microorganisms from one region of the world to another. In developing countries, many centers are more likely to treat more severe infectious keratitis because access to specialized medical centers is very limited. In these centers, patients with corneal ulcers usually present for treatment only after the infection has become well-established, sometimes weeks later when a first-line treatment has proven ineffective. Although almost two-thirds of study participants were ocular surface specialists, about one-quarter were general ophthalmologists. These proportions can also be explained by the participation of developing countries. In these countries, there is a major shortage of doctors, and several participants, particularly in Africa, shared with us the need to offer diversified care. Therefore, there are probably a lot fewer subspecialists in these areas.

In conclusion, our study provides an updated and extended view of the diagnostic and therapeutic practice patterns of BK from 54 countries around the world. These results highlight geographical disparities related to differences in socio-economic status and microbiological epidemiology among countries. Adapting our practice patterns could allow for optimizing anti-infective prescriptions, improving patients' visual prognosis, and reducing the costs of medical care, particularly for hospitalizations.

Appendix. Composition of the SMIK study group

Collaborators who participated in the study, in the creation of the questionnaire or who facilitated its distribution abroad.

1. APTEL Florent (CHU de Grenoble, Grenoble, France)
2. ARNOULD Louis (CHU de Dijon, Dijon, France)
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4. BAILLIF Stephanie (Hôpital Pasteur, Nice, France)
5. BAUDOUIN Christophe (Centre Hospitalier des Quinze-Vingts, Paris, France)
6. BOURCIER Tristan (Hôpitaux Universitaires de Strasbourg, Strasbourg, France) – Président
7. BECMEUR Pierre-Henri (Hôpitaux civils de Colmar, Colmar, France)
8. BERNHEIM Diane (CHU de Grenoble, Grenoble, France)
9. BOCKSEI Zsolt (Hôpitaux Universitaires de Strasbourg, Strasbourg, France)
10. BORDERIE Vincent (Centre Hospitalier des Quinze-Vingts, Paris, France)
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Data availability All data relevant to the study are included in the article or uploaded as supplementary information.

Declarations

Ethics approval This study was approved by the ethical committee of the French ophthalmological society (SFO) and conducted in accordance with the tenets of the Declaration of Helsinki. No patients or animal subjects were involved in this study.

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