

# Evaluation of Treatment and Management of Corneal Bacterial Ulcers – A Cross Sectional Study from Saudi Arabia

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## ABSTRACT

**Objectives:** To study the current practice patterns and opinions in the treatment of corneal bacterial ulcers among Saudi ophthalmologists.

**Methods:** A web-based online survey was conducted in Saudi Arabia to randomly selected ophthalmologists who were registered with Saudi commission for health specialties during the study period between August 2018 to December 2018 using a structured self-administered questionnaire. **Results:** Of the respondents, general ophthalmologists were 32 (58.2%) and cornea specialists were 23 (41.8%). The mean years of practice was 6.6±6.1 [mean±SD]. Among the respondents 53 (96.4%) treated corneal ulcer cases, most of them 51 (92.7%) agreed there is a relation between the use of contact lenses and ocular ulcers. Fifty respondents indicated that they prescribed antibiotics for the treatment of corneal ulcer. About 12 (52.2%) of the cornea specialist and 22 (68.8%) of general ophthalmologists prefer to use culture of ulcer (Scrapping and gram staining of ulcer) diagnostic tests prior to treatment of corneal ulcers. Fortified antibiotic used was given higher advantage and the management

of ocular ulcers differed according to the severity of each case. **Conclusion:** In conclusion, results found that the management of corneal ulcers varies from specialist to general ophthalmologist. All the respondents agreed that they prescribed two broad spectrum antibiotics to treat an advanced corneal ulcer. Additionally, most of the respondents believed that fourth generation fluoroquinolones were less effective in comparison to fortified, broad-spectrum antibiotics.

**Key words:** Corneal bacterial ulcers, Antibiotics, Fluoroquinolones, Broad spectrum antibiotics, Fortified antibiotics.

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## INTRODUCTION

Corneal bacterial ulcer is a serious eye infection that requires an early diagnosis, as well as an immediate and adequate treatment and is a significant cause of visual impairment and blindness among individual's patients.<sup>1-3</sup> A corneal ulcer is an open sore or epithelial defect with underlying inflammation of the cornea, responsible for a large proportion of post-surgery complications and severe scarring.<sup>2</sup> In many occasions, corneal scars can cause irreversible loss of clear vision, sometimes it is allergic in nature, or it can be caused by endogenous infections<sup>4</sup> or due to autoimmune disorders.<sup>5</sup> However, the corneal disease remains the leading cause of monocular blindness worldwide, especially affecting marginalized populations.<sup>2</sup> In addition, the World Health Organization (WHO) considered this disease as the main public health problem in developing countries.<sup>6</sup> According to WHO, there are about 710 corneal ulcers per 100,000 populations annually.<sup>6</sup> In India alone approximately 2 million people develop corneal ulcers every year.<sup>2</sup>

Infectious keratitis is linked to specific predisposing elements, such as poor social and economic factors including illiteracy and malnutrition.<sup>7</sup> Globally it is estimated that ocular trauma and corneal ulceration, result in 1.5 to 2 million new cases of corneal blindness annually.<sup>5</sup> Risk factors for bacterial keratitis include the use of contact lenses, physical or chemical trauma, corneal epithelial diseases, specific surgeries and immunodeficiency.<sup>8-11</sup>

The complications of corneal ulceration may lead to corneal blindness or even corneal perforation, which cannot be considered uncommon.

Fungal keratitis is a main cause for corneal blindness in Asia responsible for around 44 percent of central corneal ulcer. However, 60-70% of corneal scars or adherent Leucoma are caused by corneal ulcers which were not managed correctly, as indicated in a study carried out in India.<sup>12</sup> Organisms that introduce changes to the normal bacterial flora of the eye, such as Streptococci and Staphylococci, can defeat the defense mechanisms and cause ulceration of the cornea.<sup>13,14</sup> Right diagnosis of keratitis is important for defining an effective therapeutic plan and to control the infection. The gold standard in diagnosis remains Gram stain and culture of corneal samples despite drawbacks of this traditional method.<sup>15</sup> Determining the best treatment depends on the causative organism; however, Gram stain and culture results are usually delayed for hours and up to days, and therefore, empirical treatment is commonly started beforehand.<sup>16</sup> Topical antibiotics remain the best treatment for bacterial keratitis, and a recent review found all commonly prescribed topical antibiotics to be comparably effective.<sup>17</sup> There has been debate about the use of commercially available fourth-generation fluoroquinolones versus compounded fortified antibiotics such as vancomycin and tobramycin for the initial treatment of bacterial corneal ulcers.<sup>16,17</sup> In the United States, where bacterial resistance is rather a more complicated problem than in the developing world, fortified antibiotics have a light advantage.<sup>18,19</sup> In general, bacterial ulcers are usually responsive to treatment with available topical antibiotic drops, an increase in the rates of antibiotic-resistant infections such as methicillin-

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resistant *Staphylococcus aureus* (MRSA) in the first world are causing problems, as reported in the antibiotic resistance report performed by the Euro surveillance team.<sup>20</sup> Several randomized controlled trials have shown equivalency between the fluoroquinolones and fortified antibiotics.<sup>3</sup> Surveying several research articles, it was concluded that fluoroquinolones are the first choice for empirical treatment of bacterial keratitis, however, combined fortified antibiotics were also sufficiently effective.<sup>21</sup> This study was designed to explore the opinions of ophthalmologists regarding the management of ocular ulcers, including their approach to treatment using antibiotics and the first choice of antibiotic for several given conditions.

## SUBJECTS AND METHODS

A web-based cross sectional, nationwide survey of ophthalmologist conducted between 2018 to 2019. The study included randomly selected ophthalmologist from all the regions of Saudi Arabia including. We included ophthalmologists currently working in Saudi Arabia.

The questionnaire was prepared from extensive review of the literature published in this regard.<sup>18</sup> The questionnaire for this study composed of following group of variables, which include demographics such as region of practice, years of practice, specialties, number of corneal ulcer patients visit, Relation between the use of contact lenses and ocular ulcers, usual prescription for the ulcer patients. Second part of the questionnaire asked about Frequency of treating corneal ulcers, testing performed before treating corneal ulcers, and Frequency of corneal ulcers that were initially therapy-resistant and consisted of total of 4 questions. Thirdly it asks about opinions on the need for culturing corneal ulcers drugs of choices and dosing frequency of the antibiotics for the treatment of corneal ulcers. The questionnaire included both multiple choices and binary answer type questions. To check the validity of the questionnaire pilot study was conducted among randomly selected 3 ophthalmologists a Cronbach alpha value of 0.70 found appropriate for the study. The participants contact details were obtained from the Saudi commission for health specialty. An electronic survey designed on Google forms, an online survey tool, was e-mailed in august 2018 to randomly selected ophthalmologists, whose contact information was obtained from the Saudi Commission for the health specialties, Riyadh Saudi Arabia. The participants were sent reminders to fill and send back the surveys, to get accurate responses; reminders were sent after every two weeks to get accurate response rate. The incomplete responses and unrecognized emails and non- responders were excluded from the study. Data were anonym zed (i.e., personal information like names and addresses were removed). A unique identifier was assigned for data analysis. The data were analyzed using Statistical Package for Social Science (SPSS) Version 26 for Windows. Descriptive statistics included percentages and frequency distributions were calculated results were presented in mean± standard deviation (SD).

## RESULTS

A total of 150 surveys were distributed, 33 questionnaires failed recognize the email address of the recipient and therefore returned back to the researchers, and 62 (41%) responses were found incompletely answered, therefore were excluded from the study. Of the 150 surveys that were sent online, 55 questionnaires were completely answered, giving a response rate of 36.6%. Participants were selected randomly from 11 cities around Saudi Arabia and were either general ophthalmologists or specialized in cornea, retina or refractive surgery. Of the submitted surveys, General ophthalmologists were 32(58.2%), Cornea specialists 23(41.8%). Half of the surveyed respondents were from the central region of Saudi Arabia 27 (49.1%), while the rest were from the other regions. The minimum number of years in practice was one year and the maximum was 28 years

with a mean of 6.6±6.1 [mean±SD] years. Among the subjects almost all 53(96.4%) respondents treated corneal ulcers. Additionally, the majority of them 51 (91.1%) agreed that there is a relation between the use of contact lenses and ocular ulcers. Fifty respondents indicated that they prescribed Antibiotics for corneal ulcer patients, while 3 (5.4%) of the respondents prefer to prescribe lubricants. Further, detailed information of the responses is given in Table 1.

With regards to the number of patients requiring bacterial cultures the average was 5.2 patients with cornea specialists per month, while with general ophthalmologists the average number of patients was 3.7±3.6 [mean±SD]. An average of 6.3 patients per month, according to cornea specialists, required asking for gram stain. In addition, on average of 14.5 patients managed by cornea specialists reported resistance to initial therapy in comparison to 10.93±11.67 [mean±SD] patients managed by general ophthalmologists. About 12 (52.2%) of cornea specialists and 22 (68.8%) of general ophthalmologists preferred to use cultures of ulcer (Scrapping and gram staining of ulcer) diagnostic tests prior to treatment of corneal ulcers, while 7 (30.4%) of cornea specialists and 4 (12.5%) of general ophthalmologists reported the use of scrapping and gram staining of ulcers as diagnostic tests (Table 2).

A good majority of the respondents in both categories were reported to have a pharmacy at their workplace capable of compounding antibiotic preparations. With regards to opinions about the need for culturing corneal ulcers 25.4% of total respondents indicated that culturing corneal ulcers is always necessary (Table 3). Both non-cornea specialists, and cornea specialists specified that culturing is necessary for ulcers larger than 1.5 x 1.5 mm, regardless of the location (7 (30.4%) vs. 7 (21.8%)). Compared to general ophthalmologists, a greater number of cornea specialists stated that culturing is necessary for ulcers unresponsive to antibiotic therapy 4 (17.3%) vs 0. However, both categories of ophthalmologists agreed that culturing is necessary for ulcers larger than 1.5-1.5 mm, within the central 5 mm of the cornea (Table 3).

Study results shows that drug therapy for the treatment of corneal ulcers consisted of two treatment tiers. For the mild corneal ulcers 60% of the all respondents stated that they would use fluoroquinolones such as Moxifloxacin (39.3%) followed by Gatifloxacin (12.5%). The next most common choice among the respondents was 2 broad spectrum antibiotics, which includes cefazoline and gentamycin (18% of the respondents). (Figure 1). Regarding the First choice of antibiotics to treat an advanced corneal ulcer, 70.1% of the respondents would prefer

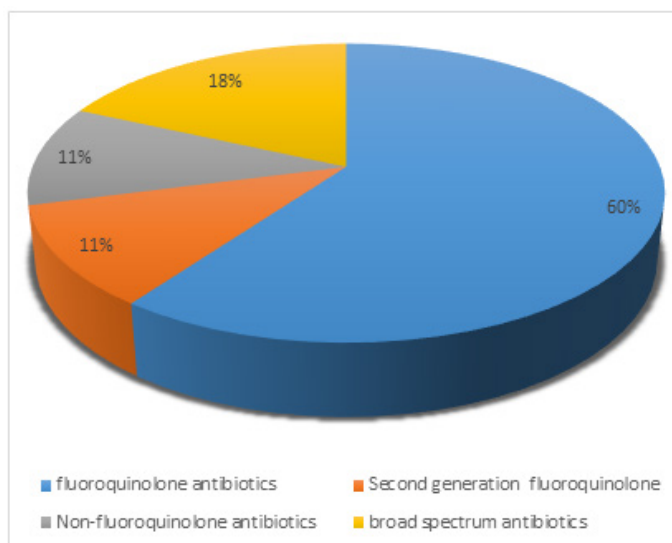


Figure 1: Shows the Initial choice of antibiotics to treat a mild corneal ulcer.

to use 2 broad spectrum antibiotics (Cefazoline and Gentamicin). The second choice among participants was Moxifloxacin (9.1%) followed by Cefazoline and other combinations (9.1%), Non-fluoroquinolone antibiotics (Tobramycin or Gentamicin) (7.2%) and Gatifloxacin (3.6%). In terms of effectiveness the comparison between fourth generation fluoroquinolones and dual, fortified, broad-spectrum antibiotics for the treatment of severe corneal ulcers, most of the respondents (64.3%) believed that fourth generation fluoroquinolones were less effective in comparison to fortified, broad-spectrum antibiotics. However, about 20 % of the respondents also believed that fourth generation fluoroquinolones are as effective as fortified antibiotics, while only 14.3% of them stated that fourth generation fluoroquinolones are better and more efficacious compared to fortified antibiotics. The detailed description of the responses is given in Table 4.

With regards to dosing frequency for the prescription of initial choice of antibiotics 33.4% of the respondents sated chose ‘every 1 hr during day and night’, 28.6% recommended the administration of antibiotics every 1 hr during the day, followed by a less number (18%) who selected ‘every 6 hr’, while ‘every 2 hr during the day’ was selected by 16.1% of the respondents. For the prescription of antibiotic more than half (57.1%) of the respondents indicated that dosing frequency would be every 1 hr during day and night, and the second most selected choice (18%) was ‘every 1 hr during the day’. More details are given in Figure 2.

## DISCUSSION

Studies on the evaluation of treatment options and opinions in the management of ophthalmologist corneal bacterial ulcers are limited. To the best of our knowledge, this is the first study which evaluate

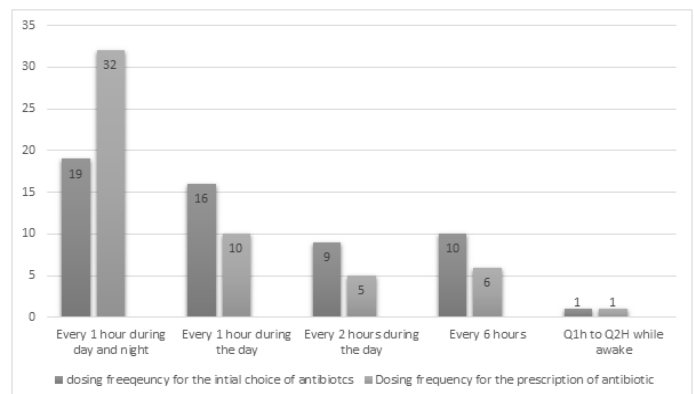
ophthalmologist’ knowledge of treatment and opinions about drug use in bacterial ulcers. This study found that 91% of the respondents agreed that a relation between the use of contact lenses and ocular ulcers. Although similar findings were reported by number of previous studies,<sup>22-26</sup> for example a study by Reddy *et al.* in 2008 reported that 78.9% of contact lenses users suffered from corneal ulcer with positive organism cultures. The contact lenses nowadays were very common and popular among individuals for the sake of beautifying the look as well as for therapeutic purposes. Although use contact lenses were found to be associated with high risk of corneal ulceration than in non- users in a number of studies around the world.<sup>22,24-26</sup>

**Table 2: Shows the Responses Listing the Frequency of Treating Corneal Ulcers, Testing Performed before Treating Corneal Ulcers, and Frequency of Corneal Ulcers That Were Initially Therapy-Resistant.**

Statements	Cornea specialists [mean±SD]	General ophthalmologists [mean±SD]
How many of corneal ulcers patients (per month) requires asking for bacterial culture?	5.2±5.4	3.7±3.6
How many of corneal ulcer patients (per month) require asking for a gram stain	6.39±12.1	3.31±3.2
When you prescribe a drug for your corneal ulcer patients, what percentage was resistant to initial therapy	14.5±16.1	10.9±11.6
Which of the following diagnostic tests do you feel is necessary prior to treatment of corneal ulcers? (Check all that apply)		
Culture of ulcer (Scrapping and gram staining of ulcer)	12(52.2)	22(68.8)
Culture of ulcer; Scrapping and gram staining of ulcer; B scan.	--	1(3.1)
Culture of ulcer; Scrapping and gram staining of ulcer; Culture of contact lenses if available.	--	1(3.1)
If resistant scrapping and gram stain	3(13)	1(3.1)
None of the above	7(30.4)	4(12.5)
Scrapping and gram staining of ulcer	---	---
Culture of ulcer	---	---

**Table 1: Survey demographics with some statements.**

Characters	n (%)
Total responses	55
Category of the ophthalmologist	
General ophthalmologists	32(58.2%)
Cornea specialists	23(41.8)
Geographic area of practice, all respondents	
Central	27(49.1)
East	14(25.1)
West	14(25.1)
Number of years in practice	6.6(SD=6.1)
Whether respondents treat corneal ulcers in practice	
Yes	53(96.4)
No	2(3.6)
On average how many corneal ulcer patients do you see per month	
General ophthalmologists (n=32)	6.0 (SD=8.45)
Cornea specialists (23)	6.8 (SD=6.4)
Relation between the use of contact lenses and ocular ulcers	
Yes	51(91.1)
No	4(7.2)
For corneal ulcer patients, you usually start with prescribing	
Antibiotics	50(89.3)
Anticholinergic	1(1.8)
Lubricant	3(5.4)
Steroids	1(1.8)



**Figure 2: Shows the dosing frequency for the prescriptions of initial choice of antibiotics and prescription of antibiotics.**

**Table 3: Shows the Opinions on the Need for Culturing Corneal Ulcers.**

Statements	Corneal specialist 23 n(%)	Ophthalmologist 32 n(%)
Is the pharmacy in your hospital capable of compounding antibiotic preparations?		
Yes	21(91.3)	26(81.3)
No	2(8.7)	6(18.8)
How often you require a culture for your corneal ulcers patients? (Check all that apply)		
Always	4(17.3)	10(31.2)
Ulcers larger than 1.5 x 1.5 mm regardless of location	7(30.4)	7(21.8)
Ulcers larger than 1.5-1.5 mm, within the central 5 mm of the cornea	10(43.4)	10(31.2)
All ulcers that extend to middle to deep stroma		
Chronic ulcers	1(4.3)	1(3.1)
Ulcers unresponsive to antibiotic therapy	3(13)	2(6.2)
Unusual patient history or clinical features	4(17.3)	0
Never	4(17.3)	1(3.1)
	1(4.3)	1(3.1)

**Table 4: Shows the choices and dosing frequency of the antibiotics for the treatment of corneal ulcers.**

Statements	n(%)
<b>What is your first choice of antibiotics to treat an advanced corneal ulcer? (Check all that apply)</b>	
Two broad spectrum antibiotics (cefazoline and gentamicin)	39(70.1)
Moxifloxacin	5(9.1)
Gatifloxacin	2(3.6)
Non-fluoroquinolone antibiotics (tobramycin or gentamicin)	4(7.2)
Cefazoline and other combinations	5(9.1)
For more severe corneal ulcers, how do you compare fourth generation fluoroquinolones with dual, fortified, broad-spectrum antibiotics	
Fourth generation fluoroquinolones are as effective as fortified antibiotics	11(19.6)
Fourth generation fluoroquinolones are better more efficacious compared to fortified antibiotics.	8(14.3)
Fourth generation fluoroquinolones are less effective	36(64.3)

Our study results reported that 89% of the surveyed ophthalmologist start with antibiotics for the treatment of corneal ulcers which is a finding in agreement with studies published in developing countries.<sup>27-29</sup> In our study about 60% of the all respondents' states that they would use fluoroquinolones for the treatment of mild corneal ulcers (Moxifloxacin 39.3% followed by Gatifloxacin 12.5%) Similar results were reported by Park J *et al.* where 55.4% of the respondents used Moxifloxacin.<sup>28</sup> Similarly, another study from 4 states in USA reported that newer fluoroquinolone antibiotics.<sup>18,29</sup> However, a study by Ariana *et al.* corneal specialists reported that only 16% of the subjects used fluoroquinolone.<sup>29</sup> These results demonstrated the good availability and effectiveness of antibiotics. In accordance with other studies, our heights of using fluoroquinolone antibiotics might be due to most effective, availability, toxicity profile and resistance to organisms.<sup>29</sup>

In our study for the treatment of advanced corneal ulcer 70.1% of the respondents would prefer to use 2 broad spectrum fortified antibiotics as the first choice which is similar to previous studies in USA where clinicians used fortified antibiotics as their initial treatment.<sup>28,29</sup> In the

present study, 17.3% of the corneal specialist always required a culture of corneal ulcers from the patients compared to general ophthalmologists (31.2%). These results were completely opposed to results of Park J *et al.* where the author reported that 12.3% of cornea specialists while 6.4% of non-cornea specialists always required cultures for corneal ulcers.<sup>28</sup> According to our study, a significant variation was found among cornea specialist and general ophthalmologist in the importance of using a culture diagnostic test of corneal keratitis as cornea specialists were more likely to do so than general ophthalmologist for ulcers larger than 1.5 x 1.5 mm regardless of location (30.4% vs 21.8%). Likewise, a study by Park J *et al.* reported that significant difference was found between corneal and non-corneal specialists regarding the use of cultures.<sup>28</sup> In fact, previous studies reported that cornea specialists were more knowledgeable in treatment of specific diseases as they have gone through this particular area more thoroughly. Additionally, other studies demonstrated the lack of availability of microbial culturing facilities and in the case of persistent large ulcers usually referred to a specialist.<sup>14,28,29</sup> Certainly, the importance of culturing is well documented in the literature. It was reported that

culturing is essential to correctly identify the etiology of infectious ulcers and to detect the specific causative organism which would help to determine the antibiotic sensitivity.<sup>30</sup>

This work showed that 64.3% of the respondents perceived that fourth-generation fluoroquinolones were less effective in comparison to fortified, broad-spectrum antibiotics for the treatment of more severe corneal ulcers. Additionally, more number of ophthalmologists, irrespective to specialty, were interested in using two broad spectrum antibiotics such as cefazoline and gentamicin for the treatment of advanced corneal ulcer. These results were consistent with previous studies<sup>22,28</sup> where participants reported that fortified antibiotics were effective for the treatment of corneal ulcers. However, other studies reported that the effectiveness of drug therapy is mainly dependent on the clinical response to a particular drug, as well as the results from the diagnostic testing through a culture of corneal ulcers.

## CONCLUSION

In conclusion, our results showed that the management of corneal ulcers differs from specialists to general ophthalmologists. All the respondents agreed on prescribing two broad spectrum antibiotics to treat advanced corneal ulcers. Although for mild corneal ulcers, most of the respondents preferred to use fluoroquinolones such as Moxifloxacin and Gatifloxacin. However, most of the respondents believed that fourth generation fluoroquinolones were less effective in comparison to fortified, broad-spectrum antibiotics. Future studies with a larger sample size are needed to investigate the effectiveness and prescribing patterns in this area is essentially important.

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## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## ABBREVIATIONS

**SD:** Standard deviation; **SPSS:** Statistical package for social science; **MRSA:** Methicillin-resistant *Staphylococcus aureus*; **WHO:** World Health Organization.

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