WORLD VIEW

Initial therapy for suppurative microbial keratitis in Iraq

Faiz I Al-Shakarchi

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See end of article for authors' affiliations

Correspondence to: Faiz I Al-Shakarchi, Ibn Al-Haetham Teaching Eye Hospital, BGW, Baghdad, Iraq; faizalshkr@yahoo.com

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Objective: To provide data-based guidelines for selection of an appropriate initial therapy for management suppurative microbial keratitis (SMK) in Iraq.

Methods: This case-series study enrolled patients with clinical signs of suppurative keratitis suspected of being microbial, presented prospectively at Ibn Al-Haetham Teaching Eye Hospital from April 2002 to March 2005. Predisposing factors, microbial profile and sensitivities of isolated bacteria were determined. If direct microscopic examination of smears was negative for fungal elements, initial therapy started with ciprofloxacin 0.3% eye-drops. Subsequent treatment depends on clinical response and cultures' results.

Results: Out of 396 cases enrolled, positive cultures were obtained in 232 cases (58.6%). The predominating agents isolated were Gram-positive cocci (*Staphylococcus* and *Streptococcus*) 75 cases (18.9%); *Pseudomonas* 68 cases (17.2%); and fungal species 74 cases (18.7%). Treatment was initiated with ciprofloxacin eye-drops in 364 cases, a favourable response was recorded in 185 cases (50.8%), addition of other antimicrobial drugs was required in 56 cases (15.4%), while failure of treatment was recorded in 123 cases (33.8%).

Conclusion: Use of ciprofloxacin eye drops alone as an initial therapy cannot cover most of the causative agents of SMK in Iraq. Addition of another drug can provide a better coverage for the predominating causative agents. The choice of this additional drug is based on the suspected infecting agent depending on the regional predisposing factors, and the clinical features.

Microbial keratitis occurs when one of the protective mechanisms of the ocular surface is disrupted.[1 2] It is a vision-threatening condition that requires urgent identification and eradication of the causative agent(s).[3 4] Microbial invasion may cause suppuration of the cornea and masking definite clinical features indicating the causative agent(s). Treatment of suppurative microbial keratitis (SMK) starts with an appropriate initial therapy[5] that depends on local contemporaneous information regarding the predominating causative organisms.[6 7]

The spectrum of micro-organisms responsible for SMK varies somewhat with regard to the geographical locations according to climatic conditions, predisposing factors and demographic characteristics of the patients.[2 8] In the developing countries, it is one of the leading causes of visual disability, with non-surgical trauma being the most important predisposing factor.[9–11] In the developed countries, the incidence of SMK had increased during the last three decades with the widespread use of contact lenses.[12–14] Corneal suppuration caused by fungi is a major public health problem in tropical regions,[15–17] while bacterial keratitis is the main cause of SMK in temperate regions.[1 18]

There is little information about SMK in Iraq as well as in the Middle East.

The aim of this study is to define the profile and predisposing factors of SMK in Iraq and then to test in vitro isolated bacterial sensitivities toward commonly used topical antibiotics in order to provide data-based guidelines for selection an appropriate initial therapy for management of SMK in Iraq.

PATIENTS AND METHODS

Setting

This study was conducted in Ibn Al-Haetham Teaching Eye Hospital, Baghdad, which is the central teaching eye hospital in Iraq with about 25 specialised ophthalmologists working there. Patients from different parts of the country can directly attend this hospital; also, it acts as a secondary and tertiary referral centre. It contains 200 beds, and more than 600 outpatients are assessed each day.

Design

This is a case series study.

Case definition and data collections

Corneal suppuration was defined as stromal infiltrate and suppuration with signs of inflammation, frequently with concurrent overlying ulceration. Microbial keratitis may or may not be associated with suppuration. This study enrolled cases of suspected microbial keratitis with suppuration, while cases of suspected microbial keratitis without suppuration (eg, viral epithelial keratitis or mild bacterial keratitis) were not included, because these cases do not usually require laboratory investigations. Hypersensitivity keratitis (eg, marginal keratitis, or Mooren ulcer) was also not included in this study.

Successive new patients attending the hospital from April 2002 to March 2005 were enrolled in this study if they had corneal suppuration presumed to be microbial. Each patient was asked about demographic features, duration of complaints, predisposing factors, therapy received prior to presentation, and associated systemic and ocular diseases. Visual acuity at presentation was recorded. Under slit-lamp visualisation, the investigating ophthalmologist examined each infected eye to document the size of the suppuration, size and depth of the concurrent ulceration, and anterior chamber reactions.

Cases were graded as severe if the suppuration or ulceration involved half or more of the corneal diameter or if the ulceration involved the deep one-third of the cornea. Other cases were graded as non-severe.

Laboratory investigations

Corneal scrapings were taken from the lesions using a sterile bent-tipped needle and were inoculated onto blood, chocolate

Abbreviation: SMK, suppurative microbial keratitis

and Sabouraud's agars, and brain–heart infusion. Further samples were taken for smears on glass slides, stained with Lactophenol cotton blue or potassium hydroxide (KOH) mounts for detection fungal elements under direct microscopic examination.

In young children, a corneal scrape was performed under general anaesthesia with operative microscope visualisation.

A definitive diagnosis of microbial keratitis was made if direct microscopic examination of smears revealed fungal elements, if there was growth of the same organism on more than one medium or if there was growth of the same organism on several ''C'' streaks on one solid medium. In a positive culture, bacteria were identified by the standard biochemical tests, while fungi were identified according to their macroscopic and microscopic appearance.

Sensitivities of isolated bacteria were tested against five antibiotics (ciprofloxacin, gentamicin, cephazolin, rifampicin and chloramphenicol) commonly used in Iraq for ocular infections. The Kirby–Bauer disc diffusion method was used, with guidelines for systemic infections according to the National Committee for Clinical Laboratory Standards (NCCLS).

Treatment

If direct smear examination was negative, ciprofloxacin 0.3% eye-drops were used as an initial therapy because they are available, they do not require reconstruction or refrigeration and they have been shown in previous studies to be effective in treating bacterial keratitis. After scrapings, all patients were admitted to the wards and received topical hourly applications of ciprofloxacin eye-drops between 7.00 am and 10.00 pm. The frequency of instillation was gradually tapered when a favourable response was recorded, whereas in poor response cases, treatment was modified according to the laboratory's tests. Due to a lack of nursing staff, applications of eye-drops were discontinued between 10.00 pm and 7.00 am. Additional sub-conjunctival injections of 20 mg of gentamicin were given for severe and sensitive cases of *Pseudomonas keratitis*, before bedtime.

Since ready-made antifungal eye-drops were not available in Iraq, cases with smears and/or culture-proven fungal infection were treated with topical amphotercin-B 0.1% drops. Fresh preparations were reconstituted every 2–4 days from the intravenous phials (Fungizone 50 mg). Antifungal eye-drops were instilled hourly during waking time.

In culture negative cases, with poor response on ciprofloxacin, treatment was switched to combined therapy of fortified cephazolin 5% and fortified gentamicin 1.4% eye-drops.

During hospitalisation, the size of the suppuration, size and depth of the ulceration, and anterior chamber reactions were measured on a daily basis. Duration of hospitalisation and follow-up after discharge were individualised as per patient requirement and response.

Signs of favourable response were: decrease in the ulcer size, blunting of its margins, decrease in suppuration and decrease in anterior chamber reactions.

Signs of treatment failure were: increase in ulcer size and suppuration with increase in the anterior chamber reaction.

The definition of healing was no fluorescein staining, no anterior chamber reaction, no or sealed perforation and replacement of the stromal suppuration by a scar.

RESULTS

Patients

During the 3 consecutive years, a total of 394 patients (396 eyes) with presumed SMK were studied. The mean age of the patients was 47.1 years, with no significant sex prevalence (male/female: 1.1/1). Most patients were from rural areas (65.2%) with agricultural employment (60.3%). At presentation, 335/396 (84.6%) cases were on topical medications (antibiotics, antiviral drugs, and/or topical steroids), and 230/396 (58.1%) cases had severe keratitis.

Laboratory investigations

Positive cultures were obtained in 232 cases (58.6%), bacteria were isolated from 162 cases (40.9%), fungi were isolated from 74 cases (18.7%), and mixed growth (fungal with bacterial co-infection) was reported in four cases. Direct smears examination was positive for fungal elements in 32 cases (43.2%), all of them were subsequently culture-proven filamentous fungal keratitis, and one case revealed concomitant bacterial growth.

Table 1 shows the profile of isolated bacteria and their sensitivities toward five antibiotics, while table 2 shows the profile of isolated fungi.

Ocular predisposing factors (table 3)

The leading predisposing factors were corneal abrasions and ocular surface disorders (dry eye, trichiasis, old scars or exposure keratitis). Most of these ocular surface disorders were sequels of cicatricial trachoma. Out of 110 culture positive cases induced by corneal abrasions, 67 cases (60.9%) were fungal, and 37 cases (33.6%) were *Pseudomonas keratitis*. Out of 83 culture positive cases predisposed by ocular surface disorders, 76 cases (91.6%) were Gram-positive cocci (*Staphylococcus* and *Streptococcus* species) keratitis, while all culture positive cases predisposed by cosmetic contact lenses (21 cases) were *Pseudomonas keratitis*.

Diabetes mellitus, a systemic risk factor for SMK, was recorded in 18 patients (19 cases); all of them had additional ocular predisposing factors. Four cases of yeast infections were reported in patients with diabetes, and three of these were mixed with bacterial co-infection.

Clinical features

A total of 76/85 (89.4%) of subsequently culture-proven Gram-positive cocci keratitis presented with concurrent clinical features of ocular surface disorders; 52/68 (76.5%) of subsequently culture-proven *Pseudomonas keratitis* presented with hyper-acute keratitis, profuse suppurations and liquefaction of the cornea; while 56/74 (75.7%) of subsequently culture-proven fungal keratitis had one or more of the following characteristics clinical signs at presentation, feathery margins or branching (hyphate) extensions from the suppurations, dry rough leathery texture or dry raised slough lesions.

Response to treatment

Initial therapy of ciprofloxacin 0.3% eye-drops was used in 364 cases with negative direct smear examination. Favourable response was recorded in 185 cases (50.8%), addition of another antimicrobial drugs was required in 56 cases (15.4%), while failure of treatment was recorded in 123 cases (33.8%). In culture-proven bacterial keratitis, additional sub-conjunctival injections of 20 mg of gentamicin were given in 52 cases with severe *Pseudomonas keratitis* according to the sensitivity test. Four cases with mixed growth responded on combination of ciprofloxacin 0.3% eye-drops and 0.1% amphotercin-B eye-drops. Treatment failure on ciprofloxacin eye-drops was recorded in 14 cases of *Streptococcus*, 8 cases of *Staphylococcus* and 6 cases of *Pseudomonas keratitis*. According to the sensitivity test, treatment switched to cephazolin 5% drops for Gram-positive cocci keratitis, and gentamicin 1.4% drops for *Pseudomonas keratitis*.

Seventy cases with culture-proven fungal infection, excluding cases with mixed growth, were treated with 0.1% amphotercin-B, and a favourable response was reported in 42

Table 1 Profile of isolated bacteria and their sensitivities toward antibiotics

		No. (%) of isolates sensitive toward each antibiotic and out of 162 cases				
Profile of isolated bacteria	**No. (%) out of 162 cases**	**Ciprofloxacin**	**Gentamicin**	**Cephazolin**	**Rifampicin**	**Chloramphenicol**
Total Gram-positive bacteria	88 (54.3%)	65	41	81	50	28
Coagulase negative *Staphylococcus*	39 (24.1%)	37	21	35	26	16
Coagulase positive *Staphylococcus*	31 (19.1%)	24	18	28	14	7
Streptococcus spp.	15 (9.3%)	1	0	15	7	3
Bacillus spp.	2 (1.2%)	2	2	2	2	2
Corynebacterium spp.	1 (0.6%)	1	0	1	1	0
Total Gram-negative bacteria	74 (45.7%)	68	61	6	2	3
Pseudomonas spp.	68 (42%)	62	55	2	0	0
Moraexella spp.	2 (1.2%)	2	2	2	2	1
Serratia spp.	2 (1.2%)	2	2	1	0	2
Nisseria gonorrhoeae	1 (0.6%)	1	1	1	0	0
Escherichia coli	1 (0.6%)	1	1	0	0	0
Total	162	133 (82.1%)	102 (63%)	87 (53.7%)	52 (32.1%)	31 (19.1%)

cases (60%). Perforation of the cornea occurred in 28 cases with poor response, and ended with phthisis bulbi (14 cases), evisceration (9 cases) or large anterior staphyloma (5 cases).

In culture negative cases, 107/164 (65.2%) cases had a favourable response to ciprofloxacin eye-drops, and treatment failure was reported in 57/164 (34.8%) cases. Treatment switched to combined fortified dual therapy in 41 cases, and a favourable response was recorded in 22 cases, all of them with pre-existing keratopathies; whereas treatment switched to 0.1% amphotercin-B eye-drops in 16 cases with clinical features of suspected fungal keratitis, and a favourable response was recorded in 9 cases.

DISCUSSION

Constructing a regional plan for management SMK requires:

(1) local contemporaneous data regarding the causative agents, their predisposing factors and sensitivities
(2) definition of the role of microbiological investigations according to the microbial profile and available laboratory's facilities
(3) choosing an appropriate initial therapy that is effective for the predominating causative agents

Microbial profile

Corneal scrapings for diagnostic culture were seldom done in Iraq, and cases of presumed SMK were treated with antibiotics not based on microbiological information. The prevalence of fungal keratitis was underestimated and any specific antifungal eye drops (eg, natamycin) were not available. The relatively high prevalence of fungal keratitis (18.7%) is related to the climatic condition and high number of agricultural employments in Iraq.

Table 2 Profile of isolated fungi

Profile of isolated fungi	**No. (%) out of 74 cases**
Aspergillus fumigatus	21
Aspergillus flavus	10
Aspergillus niger	3
Aspergillus terrus	1
Other *Aspergillus* spp.	7
Total *Aspergillus* spp.	42 (56.8%)
Fusarium oxysporium	7
Fusarium solani	6
Other *Fusarium* spp.	7
Total *Fusarium* spp.	20 (27%)
Pencillium spp.	4 (5.4%)
Scopulariopsis spp.	2 (2.7%)
Geotrichum spp.	1 (1.4%)
Alternaria spp.	1 (1.4%)
Total filamentary fungi	70 (94.6%)
Candida spp.	4 (5.4%)
Total fungi isolated	74

Most cases presented in this study were already on topical antibiotics, and this may explain the high percentage of culture-negative cases (41.5%). It is possible that *Acanthamoeba* and atypical organisms (eg, *Mycobacterium* species and *Norcardia* species) could be the cause of some of the culture-negative cases.

An important and unusual cause of SMK is induced by traditional healers or what the villages call ''mothers of haulm''. Some villagers suffering from conjunctivitis visit these women traditional healers to deal with a foreign-body sensation in their eyes, and the healers remove the ''non-existing'' foreign bodies by rubbing the cornea with a piece of cloth. Healers were not blamed if the patients had other predisposing factors. The use of cosmetic contact lenses is an increasing risk factor because most patients obtain their lenses from non-professional sellers without ocular assessments or proper hygiene care.

The NCCLS standards are based on systemic antibiotic concentrations that may not translate into a clinical treatment failure, because drug levels in the cornea that can be achieved with topical dosing may be much higher than that achieved after systemic dosing. In vitro, only 19.1% of isolated bacteria were sensitive to chloramphenicol, which was widely used in Iraq in the last three decades and sometimes the only available topical antibiotic, while 82.1% of isolated bacteria were sensitive to ciprofloxacin. Newer fluoroquinolones such as levofloxacin (third generation) and, in particular, the 8-methoxyfluoroquinolones gatifloxacin and moxifloxacin (fourth generation) offer a better coverage against Gram-positive cocci,[21 22] but regarding their availability and cost, they can be reserved for culture-proven resistant organisms only.

Microbiological investigations

The role of microbiological investigations in the management of microbial keratitis is a controversial step.[23] In regions where bacterial keratitis is predominant, many ophthalmologists treat corneal ulcers empirically without attempting to identify the causative agent, while others scrape only ulcers at risk of primary treatment failure or with an appearance suspicious of an unusual pathogen.[23–26] While in regions where the predominating causative agents can be variant types of micro-organisms (bacteria and fungi), empirical treatment with broad-spectrum antibiotics is unsatisfactory. Since there is no

Table 3 Ocular predisposing factors for SMK and their percentage out of 506

Predisposing factor	No. of isolates					Total culture positive cases	Culture negative cases	Total no. (%) out of 396 cases of SMK
	Staphylococcus keratitis	*Streptococcus keratitis*	*Pseudomonas keratitis*	Other bacteria keratitis	Fungal keratitis			
Corneal abrasions (total)	3	2	37	1	67	110	46	156 (39.4%)
Abrasions by organic materials	2		8		57	67	28	95
Abrasions induced by traditional healers			19		8	27	2	29
Other abrasions (stones, minerals, wood, fingernail	1	2	10	1	2	16	16	32
Ocular surface disorders	64	12		5	5	83***	48	131 (33.1%)
Contact lens wear			21			21	3	24 (6.1%)
Prior ocular surgery with use of topical corticosteroids	1	2			2	4*	14	18 (4.6%)
Swimming or washing in marshes or stagnant water							4	4 (1%)
Total	68	16	58	6	74	218****	115	333 (84.1%)

*Each asterisk indicates a case of mixed growth (bacteria and fungi).

one clinical feature that can be considered as absolutely pathognomonic of a particular type of aetiological agent,[27] it is recommended that every case of presumed SMK be scraped for microbiological investigations. Scraping of small lesions (smaller than 2.0 mm^2) is probably not worth while,[6] and patients with such lesions can be empirically treated. In the current study, 84.6% of cases presented were using drugs not based on microbiological investigations, and this undirectional treatment explains the high percentage of severe cases (58.1%) presented.

Previous studies have shown that Gram-stained smears are not very dependable for therapeutic decisions in bacterial keratitis,[28] whereas KOH mount smears are reliable for rapid diagnosis of fungal keratitis with high specificity.[28 29] On the other hand, direct microscopic examination requires trained personnel for detection of fungal elements and good-quality smears, which may be difficult to take in small lesions. In addition, bacterial infection cannot be detected by KOH or Lactophenol stain, and there is a possibility of bacteria co-infection with fungal keratitis[30 31] cannot be excluded.

Initial therapy

Local contemporaneous data regarding the predominating causative organisms are essential to make a rational choice for initial therapy.[32] In regions where bacterial keratitis is predominant, the initial therapy is either fluoroquinolone mono-therapy or fortified antibiotics dual therapy.[33] In the present study, Gram-positive cocci, *Pseudomonas*, and fungi species were the predominating causative agents, and constituted 227/236 (96.2%) of the total isolates. Neither ciprofloxacin monotherapy nor fortified dual therapy can provide a good coverage for these infecting agents. Fungal infections and gaps in the bacterial coverage of ciprofloxacin can be covered by addition of another drug or complementary drug. The decision as to whether to use this complementary drug is based on the suspected infecting agent depending on the regional predisposing factors and the clinical signs. Addition of a complementary drug gives a wider coverage for the possible infecting agent(s) and can provide a high concentration of an appropriate antibiotic in severe cases, taking into consideration that facilities for rapid and accurate diagnosis are not available in most hospitals in Iraq as well as in many developing countries.

If direct smear examination is negative for fungal elements, the following initial therapy is recommended for management of SMK in Iraq. In suspected fungal keratitis (history of trauma with organic materials and characteristics clinical features), the initial treatment is a combination of topical ciprofloxacin (empirical drug) and available antifungal eye-drops as a complementary drug. In suspected *Pseudomonas keratitis* (history of corneal abrasions or use of contact lenses and characteristics of the clinical features), the initial therapy can be ciprofloxacin drops (empirical drug) and in severe cases sub-conjunctival injections of gentamicin 20 mg given before bedtime, as a complementary drug. In suspected Gram-positive cocci keratitis (concurrent clinical features of ocular surface disorders), the initial therapy is ciprofloxacin drops (empirical drug) and fortified cephazolin 5% drops as a complementary drug.

Initial therapy (empirical and complementary drugs) is modified later according to the clinical response and laboratory results.

CONCLUSION

The use of ciprofloxacin eye drops alone as an initial therapy cannot cover most of the causative agents of SMK in Iraq. Addition of another drug (complementary drug) can provide a better coverage for the predominant causative agents. The decision as to whether to use this complementary drug is based on the suspected infecting agent depending on the regional predisposing factors, and the clinical features.

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REFERENCES

1 **Schaefer F**, Bruttin O, Zografos L, *et al*. Bacterial keratitis: a prospective clinical and microbiological study. *Br J Ophthalmol* 2001;**85**:842–7.
2 **Tuft SJ**. Suppurative keratitis. *Br J Ophthalmol* 2003;**87**:127.
3 **Mills R**. Corneal scraping and combination antibiotic therapy is indicated. *Br J Ophthalmol* 2003;**87**:1167–9.
4 **MacLeod SD**, LaBree LD, Tayyanipour R, *et al*. The importance of initial management in the treatment of severe infectious corneal ulcers. *Ophthalmology* 1995;**102**:1943–8.
5 **Allan BD**, Dart JK. Strategies for the management of microbial keratitis. *Br J Ophthalmol* 1995;**79**:777–86.
6 **Morlet N**, Minassian D, Butcher J, *et al*. Risk factors for treatment outcome of suspected microbial keratitis. *Br J Ophthalmol* 1999;**83**:1027–31.
7 **Leck AK**, Thomas PA, Hagan M, *et al*. Aetiology of suppurative corneal ulcers in Ghana and south India, and epidemiology of fungal keratitis. *Br J Ophthalmol* 2002;**86**:1211–5.
8 **Musch DC**, Sugar A, Meyer RF. Demographic and predisposing factors in corneal ulceration. *Arch Ophthalmol* 1983;**72**:926–30.

9 **Whitcher JP**, Srinivasan M. Corneal ulceration in the developing world—a silent epidemic. *Br J Ophthalmol* 1997;**81**:622–3.
10 **Brilliant LB**, Pokhrel PR, Grosset NC, *et al*. Epidemiology of blindness in Nepal. *Bull WHO* 1985;**63**:375–86.
11 **Upadhyay MP**, Karmacharya PC, Koirala S, *et al*. The Bhaktapur eye study: ocular trauma and antibiotic prophylaxis for the prevention of corneal ulceration in Nepal. *Br J Ophthalmol* 2001;**85**:388–92.
12 **Bourcier T**, Thomas F, Borderie V, *et al*. Bacterial keratitis: predisposing factors, clinical and microbiological review of 300 cases. *Br J Ophthalmol* 2003;**87**:834–8.
13 **Erie JC**, Nevitt MP, Hodge DO, *et al*. Incidence of ulcerative keratitis in defined population from 1950 through 1988. *Arch Ophthalmol* 1993;**111**:1665–71.
14 **Jeng BH**, McLeod SD. Microbial keratitis. *Br J Ophthalmol* 2003;**87**:805–6.
15 **Gonzales CA**, Srinivasan M, Whitcher JP, *et al*. Incidence of corneal ulceration in Madurai District, South India. *Ophthalmic Epidemiol* 1996;**3**:159–66.
16 **Hagan M**, Wright E, Newman M, *et al*. Causes of suppurative keratits in Ghana. *Br J Opthalmol* 1995;**79**:1024–8.
17 **Williams G**, Billson F, Husain R, *et al*. Microbiological diagnosis of suppurative keratitis in Bangladesh. *Br J Ophthalmol* 1987;**71**:315–21.
18 **Tuft SJ**, Matheson M. In vitro antibiotic resistance in bacterial keratitis in London. *Br J Ophthalmol* 2000;**84**:687–91.
19 **Hyndiuk RA**, Eiferman RA, Caldwell DR, *et al*. Comparison of ciprofloxacin ophthalmic solution 0.3% to fortified tobramycin-cefazolin in treating bacterial corneal ulcers. *Ophthalmology* 1996;**103**:1854–63.
20 **Leibowitz HM**. Clinical evaluation of ciprofloxacin 0.3% ophthalmic solution for treatment of bacterial keratitis. *Am J Ophthalmol*, 1991;**112**(Suppl 4), 34S–47S.
21 **Kowalski RP**, Dhaliwal DK, Karenchak LM, *et al*. Gatifloxacin and moxifloxacin: an in vitro susceptibility comparison to levofloxacin, ciprofloxacin, and ofloxacin using bacterial keratitis isolates. *Am J Ophthalmol* 2003;**136**:500–5.
22 **Parmar P**, Salman A, Kalavathy CM, *et al*. Comparison of topical gatifloxacin 0.3% and ciprofloxacin 0.3% for the treatment of bacterial keratitis. *Am J Ophthalmol* 2006;**141**:282.
23 **McDonnell PJ**, Nobe J, Gauderman WJ, *et al*. Community care of corneal ulcers. *Am J Ophthalmol* 1992;**114**:531–8.
24 **McLeod SD**, Kolahdouz-Isfahsni A, Rosamian K, *et al*. The role of smears, cultures and antibiotic sensitivity testing in the management of suspected infectious keratitis. *Ophthalmgology* 1996;**103**:23–8.
25 **McDonnell PJ**. Empirical or culture-guided therapy for microbial keratitis? *Arch Ophthalmol* 1996;**114**:84–7.
26 **Morlet N**, Daniell M. Empirical fluoroquinolone therapy is sufficient initial treatment. *Br J Ophthalmol* 2003;**87**:1169–72.
27 **Thomas PA**, Leck AK, Myatt M. Characteristic clinical features as an aid to the diagnosis of suppurative keratitis caused by filamentous fungi. *Br J Ophthalmol* 2005;**89**:1554–8.
28 **Sharma S**, Kunimoto DY, Gopinathan U, *et al*. Evaluation of corneal scraping smear examination methods in the diagnosis of bacterial and fungal keratitis: a survey of eight year of laboratory experience. *Cornea* 2002;**21**:643–7.
29 **Gopinathan U**, Garg P, Fernandes M, *et al*. The epidemiological features and laboratory results of fungal keratitis: A 10-year review at a referral eye care center in south India. *Cornea* 2002;**21**:555–9.
30 **Srinivasan M**, Gonzales CA, George C, *et al*. Epidemiology and aetiological diagnosis of corneal ulceration in Madurai, south India. *Br J Ophthalmol* 1997;**81**:965–71.
31 **Pate JC**, Jones DB, Wilhelmus KR. Prevalence and spectrum of bacterial co-infection during fungal keratitis. *Br J Ophthalmol* 2006;**90**:289–92.
32 **Daniell M**. Overview: Initial antimicrobial therapy for microbial keratitis. *Br J Ophthalmol* 2003;**87**:1172–4.
33 **Gangopadhyay N**, Daniell M, Weih L, *et al*. Fluoroquinolone and fortified antibiotics for treating bacterial corneal ulcers. *Br J Ophthalmol* 2000;**84**:378–84.