Microbial Keratitis in Thailand: A Survey of Common Practice Patterns

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Objective: *To describe the current practice patterns and prescription preferences in treating microbial keratitis in Thailand.*
Material and Method: *A questionnaire was designed and sent to ophthalmologists to describe their practice in patients with microbial keratitis. The questionnaire also presented two case scenarios with microbial keratitis; the less severe in the first patient and the more severe in the second. The recipients were asked about their diagnostic and therapeutic approaches. The surveys were mailed to 300 ophthalmologists around the country.*
Results: *One hundred and forty-three surveys (48.6%) were used in the analysis. Over half the respondents (56%) would do corneal scraping for some patients with suspected microbial keratitis. Smears and cultures of corneal specimens are the most common diagnostic tools (92%) to identify the causative organisms. Of the respondents, 60% would treat Case 1 as an outpatient, compared with 90% would admit Case 2. About half the respondents (47%) would initiate treatment in Case 1 without obtaining scrapings, whereas 79% would prefer microbial work up in Case 2. Monotherapy with topical fluoroquinolone was the most common initial antibiotic prescribed for Case 1 (36%), whereas in Case 2, combined fortified antibiotics (23%) and combined topical antibiotic and topical antifungal (22%) were preferred. For fungal keratitis, topical natamycin and amphotericin B were the most common choices (20% each).*
Conclusions: *Most Thai ophthalmologists appear to treat patients with suspected microbial keratitis differently, depending on etiology and severity. However, there are some variations in management. The validity of this approach should be established to specify patterns that are most safe and effective.*

Keywords: *Microbial keratitis, Corneal ulcer, Fungal keratitis, Survey, Practice patterns*

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Microbial keratitis is a potentially sight-threatening disorder and the leading cause of monocular blindness worldwide. In Thailand, corneal ulcers were the second most common cause of blindness according to a nationwide survey in 1994[1]. Traditional treatment has relied on first obtaining cultures and then instituting broad-spectrum therapy with multiple fortified antibiotics until causative organisms can be identified or clinical response monitored[2,3]. The management of corneal infection has evolved significantly in the last decade and there has been disparities between traditional textbook recommendations and practice, for example whether to perform corneal scraping to identify the causative organism or which antimicrobial to use for initial treatment[4]. The purpose of the present study was to identify current patterns of practice and prescription preferences of ophthalmologists in treating microbial keratitis in Thailand.

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Material and Method

The present study was approved by the Medical Ethics Committee of the Faculty of Medicine, Chiang Mai University prior to its initiation. Three

hundred ophthalmologists who were not working at any university hospitals were randomly selected from the Royal College of Thai Ophthalmology's 2002 Membership Directory.

The questionnaire consisted of 3 parts; Part 1 covered general information about recipients, including subspecialty interest and main routine practice. Part 2 covered routine practices for patients with suspected microbial keratitis, including the approximate number of patients seen in each month; whether corneal scraping was performed before initiating the treatment and whether patient education was done. Part 3 presented two hypothetical patients with suspected microbial keratitis to identify diagnostic and therapeutic approaches.

Case 1

An 18-year-old soft contact lens wearer had a one-day history of discomfort, tearing, and mild decreased vision in the right eye. The best corrected visual acuity (VA) was 6/12. There was moderate conjunctival injection, 1 x 1.2 mm stromal infiltrate outside the axis, and 1+ cell in the anterior chamber. The left eye was normal.

Case 2

A 54-year-old farmer presented with impaired vision for 4 days. A foreign body had entered his right eye while he was mowing 10 days previously. VA in the right eye was counting finger with no improvement with a pinhole. There were marked conjunctival injection, a 4 x 3 mm stromal infiltrate with an ill-defined border in the center of the cornea, and a 3 mm hypopyon. The lens and fundus could not be seen.

The following questions were asked:

- Would the respondent treat the patient or refer to another ophthalmologist?
- Would a corneal scraping be obtained before treatment?
- What would the initial antimicrobial(s) of choice be?
- If the patient were to worsen during treatment, would the respondent change the antimicrobial(s), do any diagnostic work-up, or refer the patient to another ophthalmologist?
- In Case 2, what would the preferred antifungal medication be if examination revealed filamentous fungi?

The survey was mailed to the recipients along with a self-addressed, stamped envelope and an explanatory cover letter promising anonymity. Responses were tabulated and analyzed for percentages and medians.

Results

The response rate in the present study was 49.67% (149/300). However, only 143 of the questionnaires returned were used. Six were excluded because of incomplete answers. Two respondents did not practice ophthalmology.

The distribution by location of ophthalmologists who returned the surveys is shown in Fig. 1. Most of the surveys returned (90%) came from ophthalmologists working in public hospitals. The rest (10%) were working in private hospitals. Most of the respondents (85%) were general ophthalmologists. (Fig. 2)

In routine practice, 65.7%, 19.4%, 11.9%, and 2.1% of the respondents reported seeing 1-5, 6-10, more than 10 and no cases of corneal ulcers each month, respectively. (Fig. 3) Over half the respondents (56%) would do corneal scraping as a work-up prior to treatment in some patients, particularly those with moderate to severe cases and/or suspected fungal infection. 31.9% would perform corneal scraping in all

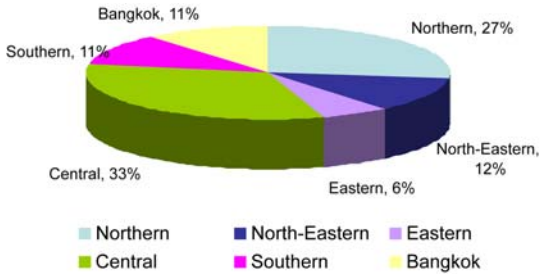

Fig. 1 Distribution of locations of respondents in Thailand

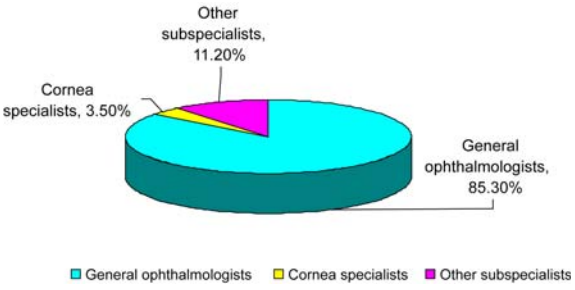

Fig. 2 Percentages of general ophthalmologists and subspecialists

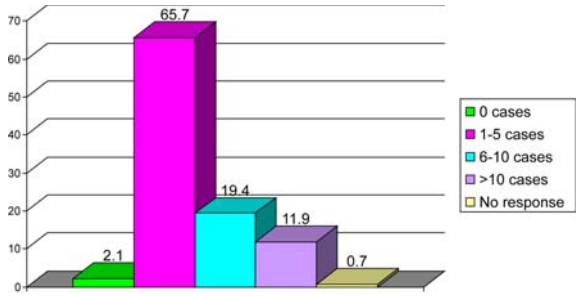

Fig. 3 Number of corneal ulcer patients seen per month

cases of suspected corneal ulcer and 12% would not do any corneal scraping at all. Smears and cultures were the most common basic laboratory tests chosen by most of the practitioners (91.5%). Patient education was done by most of the respondents (89.2%) (Table 1).

Diagnostic and therapeutic approaches for both hypothetical cases are compared in Table 2-4. Of the respondents, 59.4% would treat Case 1 as an outpatient case, whereas 89.5% would admit Case 2. About half the respondents (47.1%) would treat Case 1 with-out obtaining a corneal scraping. For Case 2, 78.7% would try to determine the causative organism before initiating treatment (Table 2).

For initial antimicrobial(s) chosen for Case 1, monotherapy with topical fluoroquinolone was chosen most often by ophthalmologists (37.8%), followed by combined therapy with fortified cefazolin and aminoglycoside (19.3%), and multiple topical antibiotics (18.6%) (Table 3).

In Case 2, the two most common treatments were combined fortified cefazolin and aminoglycoside (22.7%), and combined topical antibiotic and antifungal (22%). (Table 3) The median frequency of eye drops administration was every 1 hour in each case, ranging from 1-4 and 0.5-4 hours in Case 1 and 2, respectively.

Table 4 shows the management when the patient worsened during treatment. The two most common options for Case 1 were obtaining a corneal scraping along with modification of the antimicrobials (25%), and admission if the patient had been previously treated as an outpatient (23.5%). For Case 2, 34.1% of the respondents would modify the medications, 26.5% would refer the patient to another ophthalmologist, and 23.4% would re-scrape the lesion before modifying treatment.

For Case 2, if filamentous fungi were identified, topical natamycin and topical amphotericin B were the most common choices of practitioners (19.6% each), followed by combined topical amphotericin B and oral azole agents (12.8%) (Table 5).

Table1. Diagnostic approach and patient education for suspected infectious corneal ulcers in common practice

	n (%)
Whether corneal scraping was done before initiate treatment (n = 141)	
None	17 (12.0)
All cases	45 (31.9)
Some cases	79 (56.0)
Preference for corneal scraping (n = 79)	
1. Moderate to severe cases	28 (35.4)
2. Suspected fungal or other rare microbial infection	5 (6.3)
3. 1 & 2	39 (49.4)
4. Other	6 (7.6)
5. No response	1 (1.3)
Routine microbial work-up (n = 129)	
Smear	7 (5.4)
Culture	4 (3.1)
Smear & culture	118 (91.5)
Whether patient education was done (n = 140)	
Yes	125 (89.2)
No	15 (10.7)

Table 2. Different approaches for Case 1 and Case 2

	Case 1 n (%)	Case 2 n (%)
Status		
Outpatient	85 (59.4)	4 (2.8)
Admit	55 (38.5)	128 (89.5)
Refer	1 (0.7)	9 (6.3)
No answer	2 (1.4)	2 (1.4)
Total	143 (100)	143 (100)
Laboratory test		
No	66 (47.1)	10 (7.5)
Corneal scraping	1 (0.7)	0
Corneal scraping and smear	6 (4.3)	5 (3.7)
Corneal scraping and culture	5 (3.6)	5 (3.7)
Corneal scraping and smear & culture	38 (27.1)	104 (78.7)
Other*	24 (17.1)	8 (6.1)
Total	140 (100)	132 (100)

* Culture of contact lens and/or contact lens solution was chosen by 24 respondents for Case 1

Table 3. Initial antimicrobial(s) prescribed for Case 1 and Case 2

Initial antimicrobial therapy	Case 1, n (%)	Case 2, n (%)
Topical fluoroquinolone	53 (37.8)	6 (4.5)
Fortified cefazolin & aminoglycoside	27 (19.3)	30 (22.7)
Other single topical antibiotic*	15 (10.7)	3 (2.1)
> 1 other topical antibiotics	26 (18.6)	9 (6.8)
Topical antifungal	-	6 (4.5)
Topical antibiotic & antifungal	3 (2.14)	29 (22)
Topical & systemic antibiotic	11 (7.9)	14 (10.6)
Topical antibiotic & systemic antifungal	2 (1.4)	5 (3.8)
Topical & systemic antibiotic & topical antifungal	3 (2.1)	11 (8.3)
Topical antibiotic and topical & systemic antifungal	-	9 (6.8)
Topical & systemic antibiotic plus topical & systemic antifungal	-	4 (3.3)
Others	-	6 (4.2)
Total	140 (100)	132 (100)

* Other topical antibiotics include poly-oph, cefazolin and aminoglycoside

Table 4. Management if patient worsened during treatment

Management	Case 1, n (%)	Case 2, n (%)
Refer	20 (14.2)	35 (26.5)
Admit (if previously treated as outpatient)	33 (23.5)	2 (1.5)
Corneal scraping / re-scraping	19 (13.5)	11 (8.3)
Modify of the medication	28 (20)	45 (34.1)
Corneal scraping/re-scraping and modify medication	35 (25)	31 (23.4)
Other	5 (3.6)	8 (6.1)
Total	140 (100)	132 (100)

Table 5. Antifungal(s) prescribed for fungal corneal ulcer (n = 103)

Antifungal	n (%)
Topical natamycin	26 (19.6)
Topical amphotericin B	26 (19.6)
Topical ketoconazole	4 (3.0)
Topical natamycin and oral azoles*	9 (6.8)
Topical amphotericin B and oral azoles*	17 (12.8)
Topical ketoconazole and oral azoles*	10 (7.5)
Other**	11 (8.3)

* Oral azoles include itraconazole and fluconazole
** 5 chose topical fluconazole, and 6 referred

Discussion

The response rate in the present study was 48.6%; most respondents were general ophthalmologists working in public hospitals, so the sample should be a representative of overall ophthalmological practice in Thailand. Corneal ulcers were commonly encountered; most practitioners reported that they were seen in 1 to 5 patients each month.

In the standard approach to corneal infection, identification of the causative organism before initiating treatment is a key to its management[2,3]. About half the respondents opt to do corneal scraping prior to treatment in moderate to severe cases or when non-bacterial infection was suspected. Smears and cultures were the most common laboratory tests chosen.

Some ophthalmologists may not take scrapings for every case of corneal infection because of a good response to empirical broad spectrum therapy for mild and off-axis microbial keratitis[4]. In addition, it saves money and reduces time spent in initial evaluation if corneal scrapings are not taken. If the ulcer heals without sequelae, this approach represents substantial savings. However, failure of initial treatment increases

costs in the form of therapeutic intervention and decreases patient well-being.

Practitioners appear to approach corneal ulcers differently based upon apparent severity. A majority of the respondents would treat less severe cases as outpatients; almost all practitioners would admit severe cases into the hospital. About half the respondents would not perform corneal scraping in mild degree corneal ulcers, but most ophthalmologists would prefer to identify the causative organism in more severe cases.

Traditionally, practitioners usually use broad spectrum intensive therapy with several fortified antimicrobials until the causative organism can be identified. However, fortified antibiotics are problematic because of their toxicity, short shelf-life, and limited availability. In mild degree cases, most of the respondents would prescribe single therapy with topical fluoroquinolone initially.

Currently, topical fluoroquinolone is a widespread alternative in treating bacterial keratitis. Several trials have demonstrated clinical efficacy and safety equivalent to standard dual therapy, reduce patient discomfort, low toxicity, good ocular penetration, stability at room temperature and a requirement for hospitalization[5-7]. Recently, new varieties of fluoroquinolone have become readily available such as levofloxacin, moxifloxacin, and glatifloxacin. Some respondents in the present survey specified that they prefer these new varieties. However, with the increasing use of these antibiotics, resistance strains develop, particularly gram positive organisms[8-11]. In addition, there has been one report of an increased rate of corneal perforation where ofloxacin was used for bacterial keratitis[12].

In the second hypothetical case, which is a severe case and suspected fungal infection, conventional combined fortified antibiotics or combined topical antibiotics and antifungal treatment was equally chosen by about 20% of the practitioners as the initial treatment. This contradicts textbook guidelines, which state that antifungal agents should not be initiated without laboratory evidence because clinical history and appearance are not diagnostic, prolonged therapy is required, the response is slow and easily confused with the normal resolution of a non-fungal process, and the agents are too toxic[13]. If necessary, according to textbook guidelines, repeated scrapings or cultures should be performed to make the diagnosis.

The present survey showed that ophthalmologists preferred to prescribe antifungals as an initial treatment in cases of suspected fungal keratitis before getting the results of corneal scraping. This treatment trend may be because of the high incidence of fungal keratitis in this region[14-18], as well as the difficulty in managing it[19,20].

Treatment of fungal keratitis is currently hampered by the limited availability of effective antifungal agents for topical administration. The only commercially available topical antifungal is 5% natamycin (pimaricin). It has been recommended as the drug of choice for filamentous fungal keratitis, which is the common fungal keratitis in Thailand[15,18-20]. In this survey, topical natamycin and amphotericin B were the most common antifungals of choice (20% each). The preference for hospital-made topical amphotericin B may be because of the high cost of natamycin, which is not usually covered by the health care system in this country.

It is surprising that multiple antimicrobials including multiple topical antibiotics and/or systemic antibiotic as well as antifungals were prescribed as the initial treatment even for patients with mild severity, as in Case 1. Combined multiple antimicrobials including systemic antibiotics/antifungals were prescribed for Case 2 as well. In standard guidelines, systemic antibiotics are indicated in severe cases with impending perforation, perforation with potential intraocular spread, or scleral involvement[21,22]. Ophthalmologists should be aware of the pros and cons of empirical treatment with multiple medications. Toxicity from multiple topical agents can retard wound healing, and this may be misinterpreted as a worsening infection. An adverse reaction may occur with systemic medications, and treatment may be more expensive than it should be.

Infection of the cornea is rare in the absence of predisposing risk factors[23-26]. Common risk factors include ocular trauma, contact lens wear, ocular surface disorders, and some systemic risk factors. From this survey, it appears that most practitioners educate patients with corneal ulcers to prevent recurrence of the disease or new infections. However, patient education alone is not enough, as most cases of corneal ulcers in the developing countries including Thailand are associated with antecedent eye trauma[15-17]. Mass public education to increase awareness of specific risk factors that may predispose someone to infection is necessary to prevent the large burden of blindness attributed to corneal scarring and/or perforations.

Conclusion

A survey by mail with anonymous questionnaires can provide information about the current

practice of ophthalmologists. However, the results are based only on the responses of ophthalmologists who returned completed questionnaires. Some practitioners may give responses that indicate how they think and treat conditions covered in the survey rather than how they actually practice. On the other hand, management of microbial keratitis varies and must be modified to suit the patient.

The present results indicate that, in general, ophthalmologists have drifted away from standard textbook guidelines for management of suspected microbial keratitis. Practitioners appear to treat the patient differently, depending on etiology and severity. However, there are some variations in management among ophthalmologists. The validity of this approach should be established to identify patterns that are the safest and most effective.

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การสำรวจแนวทางการรักษาพยาบาลโรคกระจกตาติดเชื้อในประเทศไทย

นภาพร ตนานุวัฒน์, มัลลิกา สุวรรณนิพนธ์

วัตถุประสงค์: *เพื่อบอกถึงแนวทางการรักษาพยาบาลในปัจจุบันของโรคกระจกตาติดเชื้อในประเทศไทย*

วัสดุและวิธีการ: *ได้จัดทำแบบสอบถามเกี่ยวกับแนวทางทั่วไปในการรักษาพยาบาลผู้ป่วยโรคแผลติดเชื้อที่กระจกตา โดยแบบสอบถามยังได้จำลองสถานการณ์ 2 สถานการณ์ ผู้ป่วยรายแรกเป็นโรคแผลติดเชื้อที่กระจกตาที่มีความรุนแรงน้อย และรายที่สองเป็นผู้ป่วยที่มีความรุนแรงมาก โดยได้ถามถึงแนวทางในการวินิจฉัยและรักษาในผู้ป่วยทั้งสองราย จากนั้นได้ส่งแบบสอบถามไปยังจักษุแพทย์ทั่วประเทศไทย จำนวน 300 ราย*

ผลการศึกษา: *มีแบบสอบถามที่ตอบกลับมาจำนวน 143 ชุด (ร้อยละ 48.6) ที่ได้นำมาวิเคราะห์ พบว่าจักษุแพทย์กว่าครึ่ง (ร้อยละ 56) จะทำการขูดแผลที่กระจกตาไปตรวจในผู้ป่วยบางรายที่สงสัยว่ามีการติดเชื้อที่กระจกตา วิธีการตรวจหาเชื้อที่เป็นสาเหตุที่นิยมมากที่สุด (ร้อยละ 92) คือการย้อมและการเพาะเชื้อ จักษุแพทย์ร้อยละ 60 เลือกที่จะรักษาผู้ป่วยรายแรกแบบผู้ป่วยนอก ในขณะที่ร้อยละ 90 เลือกที่จะรักษาผู้ป่วยรายที่สองไว้ในโรงพยาบาล ผู้ตอบกว่าครึ่ง (ร้อยละ 47) เลือกให้การรักษาผู้ป่วยรายแรกโดยไม่ทำการตรวจหาเชื้อ ขณะที่จักษุแพทย์ร้อยละ 79 จะทำการตรวจหาเชื้อก่อนรักษาในผู้ป่วยรายที่ 2 ยาเบื้องต้นที่ถูกเลือกมากที่สุดในผู้ป่วยรายแรกคือยาหยอดตา fluoroquinolone (ร้อยละ 36) ส่วนในรายที่สองจักษุแพทย์ส่วนใหญ่เลือกให้ยาปฏิชีวนะที่เข้มข้นสองตัวร่วมกัน (ร้อยละ 23) หรือให้ยาปฏิชีวนะร่วมกับยาต้านเชื้อรา (ร้อยละ 22) ยาต้านเชื้อราที่แพทย์สั่งมากที่สุดสำหรับแผลติดเชื้อราคือ ยาหยอดตา natamycin และ amphotericin B (อย่างละร้อยละ 20)*

สรุป: *จักษุแพทย์ไทยส่วนใหญ่ให้การรักษาผู้ป่วยที่สงสัยเป็นโรคแผลติดเชื้อที่กระจกตาโดยพิจารณาตามสาเหตุและความรุนแรงของโรค อย่างไรก็ตามยังพบว่ามีความแตกต่างของการรักษา จึงควรมีการประเมินวิธีการรักษาพยาบาลดังกล่าวเพื่อหาแนวทางที่ปลอดภัยและมีประสิทธิภาพในการดูแลรักษาผู้ป่วยต่อไป*