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Research Article

Multimodal Treatment for Fungal Keratitis

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Abstract

Purpose: The feasibility of standardized treatment for fungal keratitis was explored through the analysis of results.

Methods: The medical records of 508 hospitalized patients with fungal keratitis in Qingdao eye hospital of Shandong province eye institute from January 2008 to December 2012 were analyzed in this retrospective study.

Results: Among total 508 cases (all simple eye), 21 cases (4.1%) were cured with anti-fungal drugs, 150 cases (29.5%) by debridement, 153 cases (30.1%) through lamellar Keratoplasty (LK) treatment and 162 cases (31.9%) through penetrating keratoplasty (PK) treatment. Only 4.8% patients who had ulcer infiltration depths larger than 1/2 of corneal thickness were cured by drugs or corneal ulcer debridement while the percentages of patients applied with LK and PK who had ulcer infiltration depths larger than 1/2 of corneal thickness were 91.2% and 100% relatively. Corneal ulcer diameter > 6 mm, ulcer infiltration depth > ½ of corneal thickness, and the combination of high intraocular pressure were very important influencing factors required for corneal transplantation.

Conclusions: Corneal ulcer debridement could be used as an effective scheme of early stage treatment when the ulcer infiltration depth is less than ½ of corneal thickness. LK intervention should be firmly performed when deep stromal lesions have not affected Descemet's membrane. PK could be the last defense line for the treatment of corneal fungal infection.

Keywords: *Fungal Keratitis; Debridement; Lamellar Keratoplasty; Penetrating Keratoplasty; Multimodal Treatment*

Introduction

Fungal keratitis is generally treated by means of antifungal eye drops, subconjunctival injection as well as injection into corneal stroma although the disease course could be delayed by the disadvantages of antifungal drugs such as undesirable sensitivity and corneal permeability, especially in heavier patients. Multiple reports have shown that the average healing time of fungal corneal ulcer after drug treatment was 1~2 months. After corneal ulcer was healed, corneal leukoma was left and vision was seriously affected [1-3]. Moreover, some patients had corneal perforation during ulcer treatment and must be treated by therapeutic penetrating corneal transplantation or eye excision [4-6]. Lalitha P [7] reported that approximate 31% patients with fungal keratitis experienced initial treatment failure and 61% of them had corneal perforation. For patients with corneal perforation, penetrating keratoplasty (PK) treatment should be considered although worse postoperative inflammatory response and more complications could go against the healing of corneal. Consequently it becomes the major challenge for an ophthalmologist to treat fungal keratitis effectively and reasonably while shortening disease course as well as improving prognosis.

In this paper, the clinical data of 508 patients with fungal keratitisin our hospital for 5 years from January 2008 to December 2012

were analyzed and summarized. It was concluded that corresponding treatment against fungal keratitis should be given according to the clinical characteristics of specific stages. The results of the analysis are as follows.

Patients and Methods

Patients

It was designed as a retrospective serial case study which was carried out in Qingdao eye hospital of Shandong province eye institute. The declaration of Helsinki was adhered in this study.

Inclusion criteria: patients who were diagnosed as fungal keratitis in Qingdao eye hospital and hospitalized during the 5 years from January 2008 to December 2012. Diagnostic criteria: each corneal ulcer patient who was admitted to hospital after the examination of slit lamp microscope and corneal lesion blade or clinical confocal microscopy and the diagnosis of fungal corneal ulcer could conform to any of the following requirements: (1) hyphae and/or spores were found in corneal with 10% KOH staining; (2) hyphae and/or spores were found by clinical confocal microscopy; (3) fungal culture of the corneal lesions scrape was positive. Exclusion criteria: mixed infections.

Data of all patients were analyzed retrospectively including: (1) the detailed demographic characteristics, the time range from disease initiation to visiting a doctor, the pathogenesis and previous treatment; (2) the ulcer size, infiltration depth, presence of hypopyon, presence of perforation and intraocular pressure.

The ulcer size was measured with slit lamp microscope and recorded in diameter (mm). The ulcer infiltration depth was measured by slit lamp microscope and confocal microscope.

Treatment

Drug treatment: (1) before the fungus strains were identified, an hourly dose of 5% natamycin combined with 0.5% fluconazole was given to patients and the usage frequency of drugs was reduced appropriately after improvement; (2) sensitive drug therapy was selected according to drug susceptibility results, combined with two or more kinds of common drugs; (3) after clinical cure, antifungal therapy should be continued for another 2 to 4 weeks for preventing recurrence; (4) for severe fungal infection (merged endothelial spot, hypopyon, suspicious endophthalmitis), oral itraconazole or fluconazole and sodium chloride injection intravenous drip were given along with antifungal eye drops [8].

Surgical procedure of corneal ulcer debridement was as follows. The surface moss was shaved and the organization of corneal ulcer was infiltrated with epikeratome after surface anesthesia, to determine the range of ulcer infiltration, especially the infiltrating boundary of pseudopodia; a disposable plate layer knife was used to strip the lamellar necrotic tissue about 0.5 mm around the edge of infiltration; based on the infiltrating depth, lamellar necrotic tissues could be repeatedly stripped with the sharp angle of sclera scissor to cut the steep margin into a gentle slope, so the edge of the wound after debridement could be smooth and flap, and transit to normal tissues smoothly which was conducive to corneal epithelium repairing; finally antibiotic eye ointment was applied without covering the eye and then the patient was sent back to ward for further drug therapy.

Lamellar keratoplasty (LK) and penetrating keratoplasty (PK) were all operated by experienced doctors in our hospital and the drilling range of diseased cornea was at least 0.5 mm or more than the depth of corneal ulcer infiltration. The intraoperative drilling depth of LK was deeper than lesion infiltrating depth. If the surgeon doubted that hyphae had penetrated corneal endothelium during operation then PK was necessary. After removing diseased cornea, the anterior chamber angle and iris surface or recipient bed were irrigated with 0.2% fluconazole. Once the lens was found to be infected by fungal which caused spontaneous rupture of lens capsule, extracapsular cataract extraction was performed simultaneously [8-10].

Observation indexes and statistical analysis

For patients applied with pure drug therapy and corneal ulcer debridement, the medical records should be maintained for half a year after discharge. The patients applied with PK and LK should be recorded for 1 year after surgery. The ulcer healing time of patients applied with pure drug therapy and corneal ulcer debridement was also recorded separately. The ulcer healing was defined as the condition that corneal epithelium was healed completely with sodium fluorescein staining and stromal infiltration disappearing. The recurrence rate and complications during the follow-up period were also recorded. The best corrected visual acuity and corneal state of patients applied with PK and LK were assessed one year after surgery and those of other patients were assessed six months after surgery.

Table chi-square test was used to compare the effects of corneal ulcer state on the choice of treatment. Chi-square test was used to analyze the risk factors of corneal transplantation and multiplelogistic regression analysis was used further for this purpose. The incidence of postoperative complications of LK and PK were compared by chi-square test. A P value lower than 0.05 was considered as statistically significant. Statistical software of SPSS (version 18.0) was used for analysis in Windows system.

Results

General situation

From January 2008 to December 2012, a total of 508 patients were diagnosed as fungal keratitis and hospitalized for treatment. The average age of patients were 50.8 ± 11.4 (10 ~ 81) and the average time from sickness to treatment was 22.3 ± 23.3 days (1 ~ 300 days). In all patients, 298 cases (58.7%) were male, 217 cases (42.7%) were caused by corneal trauma and the rest had no obvious causes.

The fungal culture results were positive in 413 cases (81.3%) in which Fusarium was the main pathogenic fungus in a total of 290 cases (70.2%), and the rest included *Alternaria* in 70 cases (16.9%), *Aspergillus* in 40 cases (9.7%), *Candida* in 2 cases (0.5%) and others in 18 cases (4.4%).

21 cases (4.1%) were cured with drug therapy only and the ulcer healing time was ranged from 6 to 22 days with an average value of 11.1 ± 5.1 days. 150 cases (29.5%) were treated by drugs combined with debridement and the ulcer healing time was ranged from 2 to 46 days with an average value of 12.9 ± 8.5 days. Of the eyes applied with ulcer debridement, 136 cases (90.7%) were healed after the first corneal ulcer debridement surgery and 14 cases (9.3%) through twice. The nebula would be left after corneal ulcer healing, and the cornea would be mild thin at the lesion site (Figure 1).

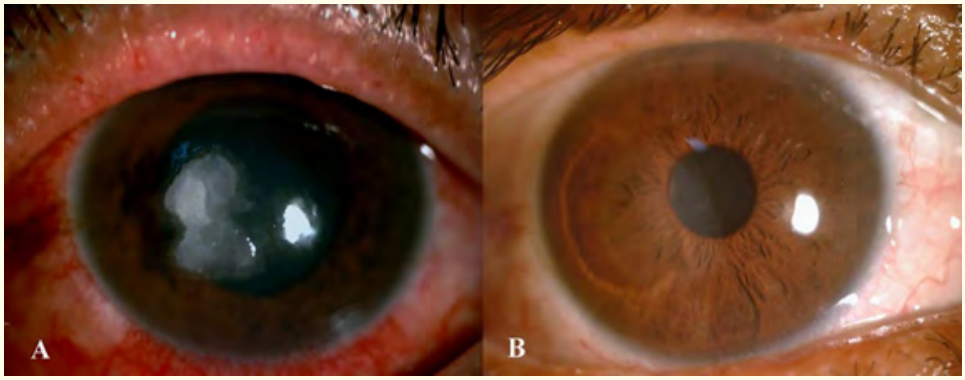

Figure 1: *(A) Fungal ulcer in an eye, with pain and decrease in visual acuity to 0.1. (B) Nebulomacular haze in the cornea 6 months after ulcer debridement; visual acuity was 0.8.*

153 cases (30.1%) were cured with LK, of which the corneal grafts of 151 cases (98.7%) remained transparent at the end of follow-up. The complications observed during the follow-up period included recurrence of fungal infection in 5 cases (3.3%), postoperative high intraocular pressure in 4 cases (2.6%), corneal graft epithelial defect in 6 cases (3.9%) as well as immune rejection in 1 case (0.7%).

162 cases (31.9%) were treated by PK, 6 cases were treated by PK in combination with intracapsular cataract extraction and 1 case was treated by PK in combination with extracapsular cataract extraction when lens infections were found in operation. Glycerol-preserved grafts were used in 34 cases (21.0%) for therapeutic transplantation due to deficiency of cornea. At the end of follow-up, the corneal graft remained transparent in 95 cases (58.6%) and the postoperative complications included postoperative recurrence of fungal infection in 7 cases (4.3%), postoperative high intraocular pressure in 26 cases (16.0%), corneal graft epithelial defects in 22 cases (13.6%) and corneal graft ulcer in 11 cases (6.8%). Fifty (39.1%) of the 128 patients applied with fresh corneal grafts exhibited immune graft rejection within 1 year after surgery (Postoperative complications of LK and PK are shown in table 1).

	N (%)	*P*-value	Management and Results
Fungal recurrence			
LK	5 (3.3)	0.771	1 cured with antifungals, 4 underwent PK
PK	7 (4.3)		5 cured with antifungals, 1 underwent secondary PK, 1 underwent enucleation because of uncontrolled fungal endophthalmitis
Postoperative raised intraocular pressure			
LK	4 (2.6)	< 0.001	4 cured medically
PK	26 (16.0)		14 cured medically, 8 cured with anterior chamber tapping, 1 cured with trabeculectomy, 3 cured with peripheral iridectomy
Graft epithelial defect			
LK	6 (3.9)	0.003	1 with medication, 5 cured with blepharorrhaphy
PK	22 (13.6)		21 cured with blepharorrhaphy, 1 underwent secondary PK
Graft ulcer			
LK	0 (0.0)		
PK	11 (6.8)		6 underwent secondary PK, 2 cured with blepharorrhaphy, 1 cured with conjunctival flap, 2 underwent evisceration because of uncontrolled endophthalmitis
Immune graft rejection			
LK	1 (0.7)	< 0.001	1 cured with corticosteroids and cyclosporine A
PK	50 (39.1) 50/128		40 cured with corticosteroids and cyclosporine A, 10 corneal endothelial decompensations

Table 1: *Complications and therapeutic results of lamellar Keratoplasty (LK) and penetrating Keratoplasty (PK).*

308 cases (60.6%) had visual acuity ≥ 0.3 after treatment, of which 78 eyes (15.4%) had visual acuity ≥ 0.8. Only 86 eyes (16.9%) had vision acuity < 0.05 and those of 114 eyes (22.4%) were 0.05 ~ 0.2 (table 2). 22 cases (4.3%) failed in treatment and eventually lost their eyeballs.

Corneal ulcer states and the selection of treatment

The patients' corneal ulcer states are shown in table 2. More than 90% patients applied with pure drugs and combined with debride-

ment had corneal ulcer diameters less than 6 mm, while the percentages of patients applied with LK and PK who had corneal ulcer diameters less than 6 mm were 56.9% and 42.6% respectively. Only 4.8% of patients with ulcer infiltrating depth > 1/2 of corneal thickness were treated by drugs or corneal ulcer debridement, while those in patients treated by LK and PK were 91.2% and 100% respectively. Consequently ulcer infiltrating depth was the key factor to decide whether corneal transplantation would be performed. The percentage of PK patients with hypopyon was 70.4%, significantly higher than those of other groups (Table 3).

	Anti-fungals	Ulcer debridement	LK	PK	Total
	N (%)	N (%)	N (%)	N (%)	N (%)
N	21	150	153	162	486
Visual acuity at the last follow-up					
< 0.05	0(0.0)	4(2.7)	1(0.7)	59(36.4)	86(16.9)
0.05~0.2	2(9.5)	14(9.3)	54(35.3)	44(27.2)	114(22.4)
≥ 0.3	19(90.5)	132(88.0)	98(64.1)	59(36.4)	308(60.6)
≥ 0.8	8(38.1)	57(38.0)	5(3.3)	8(12.9)	78(15.4)

Table 2: *Distribution of visual acuity after different treatments.*

	N	Anti-fungals	Ulcer debridement	LK	PK	P value
		N (%)	N (%)	N (%)	N (%)	
N		21	150	153	162	
Ulcer diameter						
≥ 6mm	209	2 (9.5)	5 (3.3)	66 (43.1)	93 (57.4)	< 0.001
< 6mm	277	19 (90.5)	145 (96.7)	87 (56.9)	69 (42.6)	
Depth of infiltration						
< 1/2 corneal thickness	171	17 (81.0)	139 (92.7)	15 (9.8)	0 (0.0)	
> 1/2 corneal thickness	315	4(19.0)	11(7.3)	138(91.2)	162 (100)	
Hypopyon						
Yes	180	4 (19.0)	22 (14.7)	37 (24.2)	114 (70.4)	< 0.001
No	306	17 (81.0)	128 (85.3)	116 (75.8)	48 (29.6)	
Intraocular pressure						
> 21mmHg	72	0 (0.0)	5 (3.3)	15 (9.8)	53 (32.7)	< 0.001
≤ 21mmHg	414	21 (100.0)	145 (96.7)	138 (91.2)	109 (67.3)	
Corneal perforation						
Yes	18	0 (0.0)	0 (0.0)	0 (0.0)	18 (11.1)	
No	468	21 (100.0)	150 (100.0)	153 (100.0)	144 (88.9)	

Table 3: *Comparison of different treatments for different ulcer states.*

Risk factors for corneal transplantation

According to applied treatments, all patients were divided into non-corneal transplantation group and corneal transplantation group. Chi-square test was used to conclude the risk factors for corneal transplantation as follows: the time from sickness to treatment in our hospital > 15 days (RR = 1.98, P < 0.001); ulcer diameter ≥6 mm (RR = 23.88, P < 0.001); corneal ulcer infiltrating depth > 1/2 of corneal thickness (RR = 208.0, P < 0.001); anterior chamber empyema (RR = 5.14, P < 0.001); combination of high intraocular pressure (RR = 9.14, P < 0.001) (Table 4). These risk factors were further analyzed by multiplelogistic regression and the results suggested that the factors including corneal ulcer diameter ≥ 6 mm (OR = 11.37, P < 0.001), ulcer infiltrating depth > 1/2 of corneal thickness (OR = 153.71, P < 0.001), and combination of high intraocular pressure (OR = 4.79, P = 4.79) were the most important influencing factors required for corneal transplantation. High intraocular pressure often occurred in patients with anterior chamber inflammation or anterior chamber empyema. These patients often had deeper ulcer infiltrating depth thus the risk of corneal transplantation increased accordingly (Table 5).

	Total	Non keratoplasty	keratoplasty	Risk ratio	95% CI	P Value
N	486	171	315			
Age (years)						
> 50	264	94 (35.6)	170 (64.4)	1.04	0.72 - 1.51	0.832
≤ 50	222	77 (34.7)	145 (65.3)			
The time from the sickness to treatment in our hospital (days)						
> 15	229	62 (27.1)	167 (72.9)	1.98	1.35 - 2.91	< 0.001
≤15	257	109 (42.4)	148 (57.6)			
Glucocorticoid						
Yes	20	4 (20.0)	16 (80.0)	2.23	0.74 - 6.79	0.146
No	466	167 (35.8)	299 (64.2)			
Ulcer diameter						
≥ 6mm	166	7 (4.2)	159 (95.8)	23.88	10.86 - 52.51	< 0.001
< 6mm	320	164 (51.3)	156 (48.7)			
Depth of infiltration						
< 1/2 corneal thickness	171	156 (91.2)	15 (8.8)	208.0	99.10 - 436.56	< 0.001
> 1/2 corneal thickness	315	15 (4.8)	300 (95.2)			
Hypopyon						
Yes	177	26 (14.7)	151 (85.36)	5.14	3.20 - 8.24	< 0.001
No	309	145 (46.9)	164 (53.1)			
Intraocular pressure						
> 21mmHg	73	5 (6.8)	68 (93.2)	9.14	3.61 - 23.15	< 0.001
≤21mmHg	413	166 (40.2)	247 (59.8)			

Table 4: *Analysis of risk factors for Keratoplasty.*

Variables in Regression Model	Adjusted Odds Ratio	95% CI	P value
Ulcer diameter	11.37	3.69 - 33.08	< 0.001
Depth of infiltration	153.71	69.05 - 342.19	< 0.001
Intraocular pressure	4.79	1.06 - 21.63	0.042

Table 5: *Multiple logistic regression analysis of risk factors for ketatoplasty.*

Discussion

In developing countries, fungal keratitis occupies30 ~ 60% of all infective corneal diseases [5,11-13], which is the major cause of corneal blindness. Now the medical effect for fungal keratitis is undesirable and especially worse for severe infection. Consequently medication should not be single therapy for fungal keratitis. According to the severity of patients' illness, when drug treatment is invalid, corneal ulcer debridement, LK or PK is necessary. In this paper, based on retrospective analysis of the medical records of fungal corneal ulcer patients in five years, optimal treatment option for fungal corneal ulcer in various stages of lesions was summarized and named Diversified Treatments.

Antifungal drug therapy is the first treatment that should be chosen including systemic application of itraconazole or fluconazole in combination with topical application eye drops of natamycin and amphotericin B or fluconazole. Since most patients had received unsuccessful drug treatments before coming to our hospital [5], an intensive therapy with two kinds of antifungal drugs was adopted. Most early corneal ulcer lesions with shallow infiltration were controlled well by effective drug treatment while the effect on deep stromal infiltration ulcer was usually very poor [2,3,14,15]. Bhartiya P [6] reported that the rate of eventual ulcer perforation caused by single drug treatment was 25.7%. Her P [7] proposed that the risk factors of unsuccessful drug treatment included ulcer area > 14 mm^2, anterior chamber empyema and *Aspergillus* infection. The risk factors of corneal perforation were deep ulcer of *Aspergillus* infection as well as joint anterior chamber empyema > 2 mm. According to our experience, prolonged drug treatment would not get better therapeutic effect when infected site still showed no signs of improvement after intensive treatment of antifungal drugs for 7 days. Therefore, surgical intervention should be considered as soon as possible when drug treatment was invalid to avoid further disease deterioration.

Statistical analysis suggested that the depth of corneal ulcer was one of the most important basis of operation method. Corneal ulcer debridement is a desirable treatment when ulcer infiltrating depth < 1/2 of corneal thickness. Compared with other debridement technologies mentioned in literatures by which only necrotic tissues on the surface of lesions were shaved [14], the corneal ulcer debridement in this study was used for stripping infiltrating organizations with a cornea lamellar blade to form a smooth and flat wound. This surgery could be used to increase the permeability of drugs to corneal stroma, improve drug efficacy and kill a small amount of residual hyphae on one hand and provide good conditions for corneal epithelium repairing, heal ulcer quickly and significantly shorten disease course on the other hand.

In this study, 90.7% patients applied with corneal ulcer debridement were healed in the first treatment (12.9 ± 8.5 days) and the healing time was significantly less than that of patients applied with drug treatment only as reported numerously [1-3]. Postoperative astigmatism could be reduced and satisfactory eyesight could be achieved after ulcer healing by avoiding central pupil to the greatest extent. The postoperative best corrected visual acuity was no less than 0.3 in 132 patients (88.0%) of the group.

When ulcer infiltrating depth was > 1/2 of half corneal thickness but did not reach descemet's membrane and the ulcer area was very large, LK would be an effective treatment method. LK is an important progress in the history of fungal keratitis therapy which has a significant advantage on reducing complications and improving the prognosis of visual acuity [10]. The theoretical basis of using LK to treat

fungal keratitis, surgical techniques, failure risk factors, treatment effect and so on were discussed in detail by several articles [8,10]. It was shown that the rate of postoperative corneal graft transparency rate by LK was 98.6% while that by PK was only 58.5%. Postoperative visual acuity by LK was also significantly better than that by PK. The incidence of complications by LK was much less than that by PK and postoperative recurrence rate was not significantly different between them. Consequently, on the premise of thoroughly removing infection focal, if the infection has not yet involved descemet's membrane, LK is needed for treating deep stromal lesions as soon as possible. Once the fungal hyphae penetrates descemet's membrane or corneal perforation has occurred, PK is the only effective way to save patients' eyeballs [16,17].

Most patients with fungal keratitis came from the rural areas in China where the medical conditions of basic-level hospital are relatively poor. Early diagnosis could not be realized and the understanding of fungal keratitis was not sufficient which led to misdiagnosis and improper treatments such as failing to give antifungal drugs for symptomatic treatment [5,18]. In this study, about half of the patients came to our hospital 15 days after sickness and the average time of PK group and eyeball evisceration group was 29.3 days. Four hundred and ninety-five (97.4%) patients were treated in primary hospitals, 35.6% of which experienced misdiagnosis and missed diagnosis; 4.3% were given glucocorticoid treatment which contributed to disease progress. In most patients that came to our hospital, the lesions had reached deep stromal or full-thickness infiltration and had even perforated. The opportunity of early treatment was missed and patients had to accept LK or PK treatment, even evisceration of eye in some patients.

Conclusions

It was included in this paper that for treating fungal keratitis, attention should be paid to early diagnosis and early normalized treatment. Suspected or definitely diagnosed patients should be treated with topical antifungal drugs as soon as possible. Corneal ulcer debridement could be used as an effective scheme of early treatment when drug treatment was invalid and the ulcer infiltration depth was less than 1/2 of corneal thickness. LK intervention should be firmly performed when deep stromal lesions had not involved descemet's membrane. PK is the last defense line for corneal fungal infection and could be used for the treatment of infiltration involving descemet's membrane, or already on the verge of perforation and perforated corneal ulcer, or patients who would be in danger of evisceration of eye.

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Competing Interests

The authors declare that they have no competing interests.

Contributions of Authors

Jun Cheng involved in design and conduct of the study, and preparation of the manuscript; Zhaoli Chen involved in the collection, management, analysis, and interpretation of the data; all authors review and approval of the final manuscript.

Ethics Approval and Consent to Participate

The study was approved by the ethics committee of Shandong Eye Institute and adhered to the Declaration of Helsinki.

Bibliography

1. Sharma N., *et al*. "Evaluation of intrastromal voriconazole injection in recalcitrant deep fungal keratitis: case series". *British Journal of Ophthalmology* 95.12 (2011): 1735-1737.

2. Matsumoto Y., *et al*. "The comparison of solitary topical micafungin or fluconazole application in the treatment of Candida fungal keratitis". *British Journal of Ophthalmology* 95.10 (2011): 1406-1409.

3. Yildiz EH., *et al*. "Update on fungal keratitis from 1999 to 2008". *Cornea* 29.12 (2010): 1406-1411.

4. Galarreta DJ., *et al*. "Fungal keratitis in London: microbiological and clinical evaluation". *Cornea* 26.9 (2007): 1082-1086.

5. Xie L., *et al*. "Spectrum of fungal keratitis in north China". *Ophthalmology* 113.11 (2006): 1943-1948.

6. Bhartiya P., *et al*. "Fungal keratitis in Melbourne". *Clinical and Experimental Ophthalmology* 35.2 (2007): 124-130.

7. Lalitha P., *et al*. "Risk factors for treatment outcome in fungal keratitis". *Ophthalmology* 113.4 (2006): 526-530.

8. Shi W., *et al*. "Risk factors, clinical features, and outcomes of recurrent fungal keratitis after corneal transplantation". *Ophthalmology* 117.5 (2010): 890-896.

9. Xie L., *et al*. "Treatment of fungal keratitis by penetrating keratoplasty". *British Journal of Ophthalmology* 85.9 (2001): 1070-1074.

10. Xie L., *et al*. "Lamellar keratoplasty for the treatment of fungal keratitis". *Cornea* 21.1 (2002): 33-37.

11. Chowdhary A and Singh K. "Spectrum of fungal keratitis in North India". *Cornea* 24.1 (2005): 8-15.

12. Leek AK., *et al*. "Aetiology of suppurative corneal ulcers in Ghana and South India and epidemiology of fungal keratitis". *British Journal of Ophthalmology* 86.11 (2002): 1211-1215.

13. Gopinathan U., *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* 21.6 (2002): 555-559.

14. Tuli SS. "Fungal keratitis". *Clinical Ophthalmology* 5 (2011): 275-279.

15. Behrens-Baumann W. "Keratomycosis: diagnosis and therapy". *Ophthalmologe* 106.5 (2009): 471-481.

16. Anshu A., *et al*. "Outcomes of Therapeutic Deep Lamellar Keratoplasty and Penetrating Keratoplasty for Advanced Infectious Keratitis". *Ophthalmology* 116.4 (2009): 615-623.

17. Xie L., *et al*. "Penetrating keratoplasty for corneal perforations in fungal keratitis". *Cornea* 26.2 (2007): 158-162.

18. Wang L., *et al*. "Spectrum of fungal keratitis in central China". *Clinical and Experimental Ophthalmology* 37.8 (2009): 763-771.

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