



Contents lists available at BioMedSciDirect Publications

International Journal of Biological & Medical Research

Journal homepage: www.biomedscidirect.com



Original Article

Outcome of Management of Patients with Bacterial Keratitis in Jordan

Walid N.Qubain, Ahmed E. Khatatbeh, Rame khasawneh, Asem Al-Momani

*Ophthalmologist, Department of ophthalmology, Jordanian Royal Medical Services.

** Pathologist, Department of Pathology, Jordanian Royal Medical Services.

ARTICLE INFO

Keywords:

Bacterial keratitis
Ofloxacin,
Cefazolin,
Gentamycin

ABSTRACT

Aim: to evaluate the outcome of management of patients with infective keratitis and the outcome of the culture results. **Method:** a prospective study performed in Royal Medical Services hospitals between Jan. 2009 and Jan. 2012, all patient who were clinically diagnosed to have bacterial keratitis included in this study, patient who received any type of topical or systemic antibiotics were excluded from the study, a total of 78 patients were divided into two groups; Group A patients(54 patients) are those who have infiltrates of less than 2mm in diameter and 2mm away from visual axis and less than +2 cells reaction in anterior chamber , they received a monotherapy of hourly ofloxacin eye drop, the remaining 24 patients were included in Group B and receive a combined hourly treatment of fortified gentamycin (3 mg/ml) and cefazolin (50 mg/ml), then Corneal scrapings were done and sent for culture to all patients, and the patients were admitted and followed up daily for seven days. **Results:** the mean age for all patients was 29 years, and male to female ratio was 1:1.3, group A patients with negative culture had excellent and quick response to ofloxacin monotherapy; by the 3rd day 80% of patients improved while those positive culture had excellent but delayed response to Ofloxacin, 80% improved by the 5th day of treatment. Group B patients with negative culture had excellent and quick response to combined therapy; by the 3rd day all patients improved while in those with positive culture there was excellent but delayed response to combined therapy; by the 3rd day only 60% improved but at the 6th day 90% improved. **Conclusion:** Bacterial keratitis with Small peripheral infiltrates and mild anterior chamber reaction can be effectively treated by monotherapy of ofloxacin without the need for culture, while fortified gentamycin/ cefazolin combination therapy was effective in most cases of severe forms of bacterial keratitis.

© Copyright 2010 BioMedSciDirect Publications IJBM -ISSN: 0976-6685. All rights reserved.

1. Introduction

Corneal diseases is the most common cause of legal blindness in the world after cataract and it is a common ophthalmological reason for hospital admissions (1), infective keratitis is considered the most important causes of corneal blindness (2), It is estimated that 30,000 new cases occur annually in the US [3]. the prevalence of infective keratitis is more in developing countries compared to developed countries [4,5]. very few microorganisms are capable of causing infective keratitis in normal and healthy cornea due to the presence of protective anatomical and functional mechanisms in the eye; the external epithelial layer forms a natural barrier for microorganisms , the Continuous production and flow of tears aided by the blink reflex washes and prevents the accumulation of

microorganisms, also lysozyme, lactoferrin, secretory immunoglobulins, and defensins are all present in high concentrations in tears and prevent bacterial colonization of the ocular surface [6]. A lot of factors can interrupt these normal defense mechanisms and predispose to corneal infection; wearing contact lenses, associated ocular surface diseases like dacryocystitis and blepharitis, corneal exposure to trauma, immunosuppression and surgery especially after corneal graft and refractive surgery are all considered the most common risk factors for microbial keratitis. A lot of microorganisms are capable of causing corneal infections, it can be of bacterial ,fungal, viral or protozoa origin [7], bacterial keratitis is one of the most common and important factors for infective keratitis , there is a lot of geographical variation of the causative bacteria according to the variation in the types and prevalence of risk factors [8,9,10]. early diagnosis and treatment of corneal infections is very crucial in preventing blindness and avoiding irreversible damage to the cornea. The aim of this study was to evaluate the outcome of

* Corresponding Author : Ahmed E. Khatatbeh
Ophthalmologist, Department of ophthalmology,
Jordanian Royal Medical Services
Irbid National University Irbid 2110 Po Box 2600, Amman,
Jordan
dr.r.khasawneh@gmail.com

management of patients with infective keratitis and the outcome of the culture results and whether it can affect modification and the choice of antibiotic therapy.

2. Materials and Method

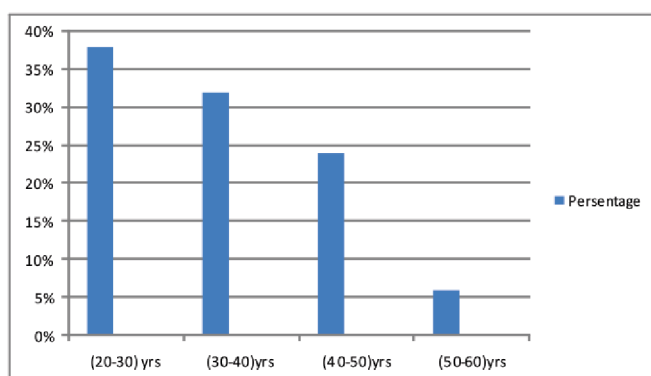
Prospective study performed in Royal Medical Services hospitals between Jan. 2009 and Jan. 2012, all patient who attend to the ophthalmology clinic and diagnosed clinically to have bacterial keratitis were included in this study ;the diagnosis of bacterial keratitis was based on clinical findings of corneal infiltrates with overlying epithelial defect and associated anterior chamber cells, patient who received any type of topical or systemic antibiotics were excluded from the study, a total of 78 patients were included in this study, detailed history was taken initially which included age, sex, presenting symptoms, past medical and surgical history, previous topical and systemic medications, history of contact lens wear and history of eye trauma, then detailed slit lamp examination of ocular external surface, anterior and posterior eye segment was performed, Corneal scrapings were obtained and sent for smear and inoculated on chocolate agar, thioglycollate broth and blood agar culture media at 35–37 °C for 24–72 hours. Patients were divided into group A and B; patients who have infiltrates of less than 2mm in diameter and 2mm away from visual axis and less than +2 cells reaction in anterior chamber were included in group A and treated with a monotherapy of hourly topical ofloxacin eye drop. The remaining patients were included in group B and received a combined hourly treatment of fortified gentmycin (3 mg/ml) and cefazolin (50 mg/ml).

Daily follow up was done and the patients were evaluated for any improvement regarding pain, visual acuity, conjunctival congestion, corneal infiltrates and anterior chamber reaction. All results obtained from the two groups were analyzed and compared.

3. Results

78 patients attended to the ophthalmology clinic and the picture was highly suggestive of bacterial keratitis , their age ranged between 23 and 58 years (mean 29 years), 44 of patients were females, figure 1 summarizes the distribution of the patients regarding to age, 54 patients were included in group A and the remaining 24 patients were included in group B, in all cases the most prominent presenting symptom was eye pain.

Figure -1



in all patients 58 patients(74%) showed positive culture; 20 of them were from group A and the remaining 38 were from group B. Table 1 and 2 summarizes the number of the patients with positive and negative cultures improved upon regular daily follow up in group A and B respectively.

Table 1

	Positive culture(38/54)	Negative culture(16/54)
1st day after treatment	3/38	6/16
2nd day after treatment	6/38	10/16
3rd day after treatment	19/38	13/16
4th day after treatment	30/38	16/16
5th day after treatment	30/38	16/16
6th day after treatment	34/38	16/16
7th day after treatment	35/38	16/16

It is worth to mention that in group A two patients on the 4th day after treatment and one patients on the 5th day with positive cultures infiltrates increased in size and became more than 2mm in size associated with increase anterior chamber reaction and so the patients were shifted to combined fortified therapy. Also 2 patients the result of the culture was resistant to ofloxacin although they improved clinically and the same treatment continued.

Table 2

	Positive culture(20/24)	Negative culture(4/24)
1st day after treatment	1/20	1/4
2nd day after treatment	6/20	2/4
3rd day after treatment	12/20	4/4
4th day after treatment	14/20	4/4
5th day after treatment	16/20	4/4
6th day after treatment	18/20	4/4
7th day after treatment	18/20	4/4

In group B four patients showed worsening of the symptoms by the 3rd day and the culture result for them revealed resistance to cefazolin which was replaced by vancomycin or ceftazidime according to the culture result but two of those continued without improvement until the 6th day and so was referred to a corneal specialist for assessment and possible corneal biopsy.

Regarding the presence of predisposing factors for infective keratitis , 23 of patients showed no risk factors by history and examination, 18 of them had negative culture and 5 of them belonged to group A positive culture patients, while the remaining 55 patients; 27 of them had history of contact lens wear, 21 patients had history of trauma, 5 of them had recent history of eye surgery and 2 had associated blepharitis with rubbing eye lashes.

50% of patient with positive cultures revealed gram positive organisms; Staphylococcus aureus and Streptococcus pneumonia accounted for the majority of cases, 45% showed gram negative organisms mainly Pseudomonas aeruginosa and 5% showed mixed growth.

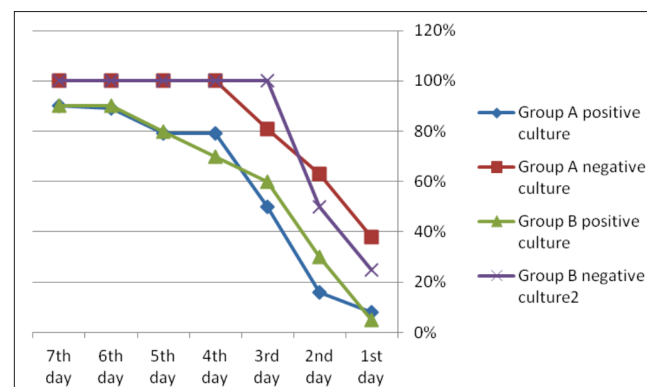
4. Discussion

Microbial keratitis is a very important cause of ocular morbidity and avoidable visual impairment and continues to be a common reason for hospital admissions in ophthalmology. Early diagnosis and identification of the causative organism helps to aid in more efficient treatment that hasten the speed of recovery, decrease the associated morbidity and prevent irreversible corneal damage.

70% of patients with bacterial keratitis aged between 20 and 40 years, that's probably because those are more vulnerable to risk factors like contact lens and trauma which accounted for 87% (48/55) of the patients with risk factors included in this study, in a study performed in France by Bouncier et al. it was founded that the main age of patients with bacterial keratitis was 39 years with male to female ratio of 1:1 (11), in our study the mean age was 29 years with male to female ratio of 1:1.3, this difference is due to the fact that life expectancy in France is higher than in Jordan and the highest patient's age included in Bouncer's study reached 98 years compared to 58 years in our study, and the higher female to male ratio in our study is probably because wearing contact lens is much more prevalent among females rather than males in Jordan unlike France in which it is prevalent among both sexes. Regarding the presence of predisposing factors; contact lens wear (35%) and trauma (27%) were the major risk factors among the whole patients. Many studies have shown that contact lens wear followed by trauma are major risks for bacterial keratitis (11). Taking in consideration that 29% of patients had no known risk factor, most of them (78%) revealed negative culture of corneal scraping, this rise the possibility misdiagnosing marginal keratitis as bacterial keratitis.

The percentage of positive culture growth vary among studies, in our study patients 58 patients (74%) showed positive culture, this result was very near to that done in India by Bharathi et al. in which positive culture was obtained in about 70% of patients (12), unlike another study done by Zhang et al. in which positive cultures found in only 14% of the corneal scrabs (13), but Zhang et al. used only blood agar plate to culture the specimens. 20 of patients with positive culture were from group B and constituted around 83% of them, while the remaining 38 were from group A and constituted around 70% of them, this mostly due to the smaller size of the infiltrates in group A compared to that of group B and higher possibility to have ineffective and inadequate corneal scrabs, in addition to that there is higher possibility of misdiagnosing marginal keratitis as bacterial keratitis in group A patients. Although our study showed a lower percentage of gram positive organisms than other studies (11), but it showed that Staphylococcus aureus, Streptococcus pneumonia and Pseudomonas aeruginosa accounted for the majority of cases, which support the results obtained by other studies (2).

Figure 2 summarizes the percentage of the patients improved on daily follow up in group A and B patients with positive and negative culture results.



Group A patients with negative culture had excellent and quick response to ofloxacin monotherapy; by the 3rd day 80% of patients improved, signs of improvement includes⁽¹⁴⁾

- Reduction in pain.
- Reduced amount of discharge.
- Lessened eyelid edema or conjunctival injection.
- Decreased density of the stromal infiltrate in the absence of progressive stromal loss.
- Reduced stromal edema and endothelial inflammatory plaque.
- Consolidation and sharper demarcation of the perimeter of the stromal infiltrate.
- Reduced anterior chamber cell, fibrin, or hypopyon.
- Initial re-epithelialisation.
- Cessation of progressive corneal thinning.

In group A patients with positive culture there was excellent but delayed response to ofloxacin, the percentage of patients who improved was only 50% on the 3rd day but at the 5th day it was 80%, taking in consideration that in 3 patients of this group the infiltrates increased in size and became more than 2mm in size with anterior chamber reaction and so the patients were shifted to combined fortified therapy, the percentage of patients who continued on ofloxacin and improved at 5th, 6th and 7th day will be 87%, 97% and 100% respectively, even patient whom culture showed resistance to ofloxacin improved with drug installation. Ofloxacin is considered one of the 2nd generation quinolones it has a broad spectrum of action and act by inhibiting the synthesis of the bacterial DNA. Many studies proved that ofloxacin is highly effective against pseudomonas (15) and suitable for most staphylococcal species (16), these two micro organisms form a large proportion of bacterial keratitis, our study also showed that ofloxacin is very effective alone for treatment of early forms of bacterial keratitis. Hyndiuk (17) compared the effect of monotherapy treatment to combined therapy and showed no difference in the outcome between the two.

The culture results did not alter the treatment of patients in group A because all patients respond well to treatment with ofloxacin even when the micro organism showed to be resistant to the drug on the culture result. This suggests that early and mild forms of bacterial keratitis can be successfully treated with ofloxacin monotherapy without the need for doing culture.

Group B patients with negative culture had excellent and quick response. Combined therapy, by the 3rd day all patients improvement, while those with positive culture there was excellent but delayed response to combined therapy; by the 3rd day only 60% improved but at the 6th day 90% improved. Cefazolin is one of the cephalosporins it is effective against gram positive cocci (14) while gentamycin belongs to the aminoglycosides group and it is highly effective against *Pseudomonas* (18), so by using the combined therapy most of the micro organisms causing bacterial keratitis are covered. Four patients in group B showed worsening of the symptoms by the 3rd day and the culture result for them revealed resistance to cefazolin which was replaced by vancomycin or ceftazidime according to the culture result but two of those continued without improvement until the 6th day and so was referred to a corneal specialist for assessment and possible corneal biopsy. So patient with no improvement by the 3rd day or those who have worsening of the eye condition review of the causative micro organism and the antibiotic susceptibility is essential for modification of the treatment and if this condition continue reviewing the diagnosis of bacterial keratitis by a corneal specialist is required. Although fortified cefazolin and gentamycin are not available as commercial products and have short shelf life with some toxic effect to the corneal epithelium but it was found to be highly effective in patients with severe forms of bacterial keratitis which will have positive impact on the outcome of bacterial keratitis and prevent irreversible damage to the cornea.

5. Conclusion

Bacterial keratitis with Small peripheral infiltrates and mild anterior chamber reaction can be effectively treated by monotherapy of ofloxacin without the need for culture, while combined cefazolin/gentamycin combination therapy was effective in most cases of severe forms of bacterial keratitis.

6. Reference

- [1] Whitcher JP, Srinivasan M, Upadhyay MP. Corneal blindness: a global perspective. *Bull World Health Organ*. 2001;79(3):214-21.
- [2] Abdullah M., Nadiya K., Archana T. Bacterial Keratitis: Perspective on Epidemiology, Clinico-Pathogenesis, Diagnosis and Treatment. *Sultan Qaboos Univ Med J*. 2009 August; 9(2): 184-195.
- [3] Erie JC, Nevitt MP, Hodge DO, Ballard DJ. Incidence of ulcerative keratitis in a defined population from 1950 through 1988. *Arch Ophthalmol*. 1993;111:1665-71.
- [4] Upadhyay MP, Karamcharya PC, Koirala S, Shah DN, Shakya S, Shrestha JK, et al. The Bhaktapur eye study: Ocular trauma and antibiotic prophylaxis for the prevention of corneal ulcers in Nepal. *Br J Ophthalmol*. 2001;85:388-92.
- [5] Ormerod LD, Hertzmark E, Gomez DS, Stabiner RG, Schanzlin DJ, Smith RE. Epidemiology of Microbial keratitis in Southern California. *Ophthalmology*. 1987;94:1322-33.
- [6] Ramesh S, Ramakrishnan R, Bharathi MJ, Amuthan M, Viswanathan S. Prevalence of bacterial pathogens causing ocular infections in South India. *Indian J Pathol Microbiol* 2010;53:281-6
- [7] Usha G., Savitri S., Prashant G. and Gullapalli N. Review of epidemiological features, microbiological diagnosis and treatment outcome of microbial keratitis: Experience of over a decade. *Indian J Ophthalmol*. 2009 Jul-Aug; 57(4): 273-279
- [8] Ormerod LD, Hertzmark E, Gomez DS, Stabiner RG, Schanzlin DJ, Smith RE. Epidemiology of Microbial keratitis in Southern California. *Ophthalmology*. 1987;94:1322-33.
- [9] Vajpayee RB, Dada T, Saxena R, et al. Study of the first contact management profile of cases of infectious keratitis: a hospital-based study. *Cornea* 2000;19:52-6.
- [10] Neumann M, Sjostrand J. Central microbial keratitis in a Swedish city population. *Acta Ophthalmol Copenh*. 1993;71:160-4
- [11] T Bourcier, F Thomas, V Borderie, et al. Bacterial keratitis: predisposing factors, clinical and microbiological review of 300 cases. *Br J Ophthalmol*. 2003 July; 87(7): 834-838.
- [12] M J Bharathi, R Ramakrishnan, R Meenakshi, et al. Microbiological diagnosis of infective keratitis: comparative evaluation of direct microscopy and culture results. *Br J Ophthalmol*. 2006 October; 90(10): 1271-1276.
- [13] Chen Zhang, Yanchuang Liang, Shijing Deng, et al. Distribution of bacterial keratitis and emerging resistance to antibiotics in China from 2001 to 2004. *Clin Ophthalmol*. 2008 September; 2(3): 575-579.
- [14] AAO(American Academy of ophthalmology). BCSC External disease and Cornea 2007-2008;8:179-185.
- [15] Ofloxacin Study Group. Ofloxacin monotherapy for the primary treatment of microbial keratitis. *Ophthalmology* 1997;104:1902-9.
- [16] M Daniell. Overview: Initial antimicrobial therapy for microbial keratitis. *Br J Ophthalmol*. 2003 September; 87(9): 1172-1174.
- [17] Hyndiuk RA, et al. *Ophthalmology*. 1996;103:1854-1863.
- [18] Gales AC, Jones RN, Turnbridge J, et al. Characterisation of *Pseudomonas aeruginosa* isolates: occurrence rates, anti-microbial susceptibility patterns and molecular typing in the Global Sentry Anti-Microbial Surveillance Programme 1997-1999. *Clin Infect Dis* 2001;32(Suppl 2):S146-55