Original Article

Antibiotic Susceptibility Patterns of Pseudomonas Corneal Ulcers in Contact Lens Wearers

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ABSTRACT

Purpose: To evaluate the resistance or susceptibility of *Pseudomonas aeruginosa*, the most common pathogen in contact lens keratitis and corneal ulcer, to different antibiotic regimens. **Materials and Methods:** This cross-sectional study included all patients with recently diagnosed contact lens corneal ulcer whose culture results were positive for *P. aeruginosa*, from March 2009 to March 2010. The empirical antibiotic therapy was changed to appropriate antibiotics according to the culture results, provided that satisfactory clinical improvement was not achieved with the initial antibiotic regimen. The overall sensitivity or resistance of *P. aeruginosa* to the most commonly used antibiotics was assessed based on the results of the antibiograms. **Results:** Fifty-two patients (43 females and 9 males) were included. Forty-five patients (86%) were wearing cosmetic contact lenses, while 7 patients (14%) were using therapeutic contact lenses. Thirty-nine patients (75%) were hospitalized and 13 patients (25%) were followed up through an outpatient clinic. Thirty patients (58%) had central ulcers, whereas 22 patients (42%) had peripheral ulcers. Twelve patients (23%) had hypopyon in their first exam. The mean time to diagnose the ulcer after the last time wearing was 2 days (range: 12 hours to 5 days). AMT was required for 10 patients (19%). Based on the antibiograms, PA was shown to be sensitive in 100% of cases to ceftazidime and ciprofloxacin. Amikacin, imipenem, and gentamicin were the second most effective antibiotics. **Conclusion:** *P. aeruginosa* was highly sensitive to ceftazidime, ciprofloxacin, and amikacin. All cases were resistant to cefazolin. Resistance to multiple antibiotics might be a significant concern in patients with corneal ulcers. In referral centers dealing with corneal ulcers, the initial antibiotic regimens should be changed from time to time to prevent this phenomenon.

Key words: Antibiogram, Antibiotic Resistance, Corneal Ulcer, Contact Lens, Keratitis

INTRODUCTION

Pseudomonas aeruginosa is the leading cause of contact lens-induced keratitis and corneal ulcers.[1] *P. aeruginosa* is a gram-negative bacterium, which typically produces a sweet odor which makes it possible to distinguish the bacterium from other bacteria in culture. In most organs, such as lungs, urinary tract, etc, *P. aeruginosa* is considered an opportunistic pathogen with a tendency to cause infections in immune-compromised patients. Likewise immune-compromised environments within

the eye, such as cornea, aqueous humor, and vitreous humor may also be a host. In the eye, extracellular enzymes cause a rapidly destructive lesion, which may lead to keratitis, corneal ulcer, and endophthalmitis.

Some predisposing factors such as trauma, contact lens wear, ocular diseases, and intensive care unit hospitalization may play a role in the development of corneal ulcers.[2] Among these factors, contact lens-associated keratitis and corneal ulcers are of the utmost importance as they may lead to cellulitis or

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endophthalmitis causing devastating disability in an otherwise healthy patient.

It is common practice to choose the empirical antibiotic therapy against *P. aeruginosa* in contact lens ulcers until the results of culture are known. We use this approach in our center however potential for the development of antibiotic-resistant strain of *P. aeruginosa* remains a concern. The hospital where our center is based is one of the main referral hospitals in the country and the Middle East.

The purpose of this cross-sectional study was to determine the efficacy of empirical antibiotic therapy as the initial treatment for contact lens-induced corneal ulcers and to compare the results of antibiograms regarding the most effective initial antibiotic regimen.

MATERIALS AND METHODS

This cross-sectional study included all patients with contact lens-induced corneal ulcers who were admitted to our center from March 2009 to 2010. After the initial screening, 52 subjects including 9 males and 43 females whose culture results were positive for *P. aeruginosa* were recruited into the study. In our center the routine practice for cases with corneal ulcers is to perform smears for gram stain and then culture the specimens in three different mediums: blood agar, chocolate agar, and saburode (for fungal infections). When the culture becomes positive for bacterial keratitis after 72 h, the antibiogram and susceptibility are determined within the Mueller-Hinton media.

All subjects were soft contact lenses wearers using either disposable extended-wear lenses or conventional daily soft contact lenses. The disinfection regimen included hydrogen peroxide or no hygiene regimen.

RESULTS

The mean age of the cohort was 21.5 years old (range: 17-31 years). In 39 subjects (75%), an empirical antibiotic regimen was recommended including fortified ceftazidime and vancomycin (every 5 min for the first hour and then hourly) at presentation and immediately after corneal scrapings for sensitivity testing. Small eccentric (2×2 mm or less) ulcers (13 patients (25%)) were prescribed ciprofloxacin every hour after corneal scrapings were performed. The regimen continued for all subjects over 72 h and then tapered once the patient and the physician noted an effective clinical response. Cases in which there was no change in the size of the ulcer and no clinical response after 72 h received a new antibiotic regimen based on the results of the antibiogram. Some patients underwent amniotic membrane transplantation. Cases prescribed ceftriaxone and carbenicillin were excluded from the study, due to inadequate sample size for comparison.

Forty-five (86%) subjects were disposable daily lenses wearers, while 7 subjects (14%) wore conventional daily contact lenses. Twenty (38%) subjects used hydrogen peroxide for disinfection of contact lenses, whereas 32 (62%) used no disinfection regimen.

Thirty-nine (75%) subjects were hospitalized, while 13 subjects (25%) were followed in an outpatient clinic. None of the latter group of subjects required hospitalization during the follow up.

The ulcer size was 2 or less than 2 mm^2 in 13 subjects (25%), 2 to 3 mm^2 in 23 subjects (44%), and more than 3 mm^2 in 16 subjects (31%). Thirty subjects (58%) had central ulcers, whereas 22 subjects (42%) had peripheral ulcers. Hypopyon was present in 12 (23%) subjects at initial presentation. The mean time to diagnose the ulcer after last wear of contact lenses was 2 days (range, 12 h to 5 days).

A successful clinical response of 81% was observed in the cohort with the prescribed antibiotic therapy. Amniotic membrane transplantation was required in 10 subjects (19%) with a mean age was 21 years old and the mean size corneal ulcer of 4×4 mm. Hypopyon was present in 58% of subjects who required amniotic membrane transplantation.

The antibiogram results indicated that 100% of the cases of *P. aeruginosa* were sensitive to ceftazidime and ciprofloxacin, whereas amikacin, imipenem, and gentamicin were the second most effective antibiotics [Table 1].

DISCUSSION

Contact lens wearers are at increased risk for the development of bacterial keratitis and corneal ulcers.[3,4] *P. aeruginosa* is the most common cause of contact lens-related ulcers.[5] *P. aeruginosa* tends to adhere to the surface of the contact lens and is transferred through damaged corneal epithelium penetrating deeper layers of the cornea and causing corneal ulcers. A severe infection can cause permanent blindness.

Previous studies have estimated the incidence of bacterial

Table 1: Antibiogram results for the sensitivity and resistance of *Pseudomonas aeruginosa*		
Antibiotic	Sensitive (%)	Resistant (%)
Amikacin	97	3
Cefazolin	0	100
Ceftazidime	100	0
Chloramphenicol	3	97
Ciprofloxacin	100	0
Gentamicin	93	7
Imipenem	96	4
Tetracycline	29	71
Trimethoprim	4	96
Vancomycin	0	100

keratitis from 2/100,000 yearly for rigid contact lens, 2.2-4.1/100,000 per year for daily wear soft contact lens and 13.3-20.9/10,000 per year for extended-wear soft contact lenses.[4-7] The risk with therapeutic contact lenses is even higher at approximately 52/10,000 yearly.[6] Some authors[6] believe that the introduction of silicone hydrogel contact lenses (which can be worn up for 30 nights) and daily disposable contact lenses have changed the incidence of corneal infection and that newer studies are warranted for accurate estimates of contact lens-induced keratitis and corneal ulcer.

The major risk factors for microbial keratitis and corneal ulcer are overnight wear, smoking, male gender, and socioeconomic factors.[4,6-8] The current study found a greater number of female subjects than males with corneal ulcers. However a conclusion on the possible role of gender as a risk factor from the results of the current study is not possible due the small sample size. Advertising campaigns encouraging the use of colored contact lenses as a fashion accessory for women may have resulted in greater use of contact lens that may explain the discrepancy between our study and previous studies.

Preventive methods that decrease the risk of *Pseudomonas*-induced keratitis are being actively investigated. To date, the efficacy of these preventive strategies remains unproven. These methods include alternative disinfecting systems, silver-containing contact lenses, antimicrobial chitosan, polyquats, cationic peptides, and selenium.[9] Although the current widespread use of cosmetic contact lenses and the threat of keratitis even under the best conditions are of great concerns, the introduction of disinfecting systems may help to decrease the infection rate in the future.

Clinically, treatment failure might be surmised by some predisposing factors such old age, medium or large ulcers, hypopyon, and poor visual acuity.[10] The current study confirms the possible role of hypopyon and the large size of the ulcer, both of which were dramatically higher in the group of patients who underwent amniotic membrane transplants during the course of their treatment (19% of patients). We cannot comment on the possible role of old age or visual acuity, as these two factors were not considered in the current study.

Pinna *et al,*[1] reported that multiple antibiotic resistance was present in all strains of *P. aeruginosa*, while the susceptibility rate was 100% to aminoglycosides and fluoroquinolones. This was also confirmed by Ly *et al,*[10] who found out that most corneal ulcers were sensitive to ciprofloxacin and aminoglycosides. In the current study, nearly all cases were resistant to more than four antibiotics, while sensitivity to ceftazidime and ciprofloxacin was 100%. Interestingly, resistance to cefazolin and vancomycin was observed in all subjects in the currently study. Currently no single antibiotic is effective against all bacterial species causing microbial keratitis. Initial broad-spectrum therapy is

recommended until the offending microorganism is identified in culture. Combination therapy with an antibiotic active against gram-positive bacteria (e.g., vancomycin, bacitracin, neosporin, cefuroxime, or cefazolin) and an agent active against gram-negative bacteria (e.g., tobramycin, gentamicin, amikacin, ceftazidime, ciprofloxacin, levofloxacin, or ofloxacin) provides good initial broad-spectrum antibiotic coverage. Although vancomycin is an anti-staphylococcal antibiotic to which resistance is rarely seen, its use should be reserved for the treatment of staphylococcal infections resistant to all other antibiotics.

Although some authors suggest the fortification of the first generation of cephalosporins with aminoglycosides as an effective initial treatment in corneal ulcers[9] our study strongly suggest that cefazolin in not efficacious in these patients. The results of the current study suggest the concurrent use of ceftazidime and amicacin or ceftazidime and ciprofloxacin as the initial treatment. An alternate antibiotic regimen should be considered in patients who do not show clinical response or who develop toxicity from the agent(s) prescribed for initial therapy. Antimicrobial sensitivity testing facilitates the selection of appropriate agents for this group of patients. This therapeutic approach is necessary to reduce the development of strains resistant to nearly all antibiotics.

The following clinical parameters are useful in monitoring the clinical response to antibiotic therapy: blunting of the perimeter of the stromal infiltrate, decreased density of the stromal infiltrate, reduction of stromal edema and endothelial inflammatory plaque, reduction in anterior chamber inflammation, reepithelialization, and cessation of corneal thinning. The frequency of topical antibiotic administration should slowly be tapered as the stromal inflammation resolves.

In the current study, almost the entire cohort was resistant to chloramphenicol, trimethoprim, vancomycin, and cefazolin. Hence, we suggest these antibiotics should not be included in any empirical antibiotic regimen against *P. aeruginosa*. Resistance to chloramphenicol has been previously reorted.[11]

Even with optimal contact lens care and hygiene, keratitis seems to be inevitable in patients who wear contact lenses. The problem might be more common in patients who wear cosmetic contact lenses in comparison to patients who wear lenses for therapeutic reasons. In the current study, 45 (86%) of the subjects had corneal ulcers after wearing cosmetic lenses. One reason for this large discrepancy might be that contact lens dispensers spend less in teaching cosmetic lens wearers about contact lens hygiene compared to patients who were therapeutic contact lens wearers. Additionally, follow-up visits are usually absent for cosmetic lens wearer. Hence, once cosmetic lens wearer is symptomatic, there is an increased tendency to use topical

steroids without the consultation from an ophthalmologist which may finally lead to a well-established corneal ulcer.

A group of cosmetic colored contact lenses which can be purchased via non-professional suppliers were the major source of corneal ulcers in the current study. In most countries, a person who is not a medical practitioner or registered optician should not sell the contact lenses; however this act does not include the purchase of the cosmetic Plano (or Afocal) contact lenses, which have no optical power. Recent reports of equal potential complications in both types of contact lenses (therapeutic or cosmetic) [12] indicates that all types of contact lenses should be fit only by a registered medical practitioner or registered opticians. We concur with this position due to the high prevalence of corneal ulcers in this group of patients in our study. All the patients wearing contact lenses and especially cosmetic lens wearers should be familiar with simple preventive hygiene such as hand washing prior to handling the lenses and using disinfection agents.

In conclusion, prompt diagnosis of keratitis and corneal ulcers and treatment with appropriate antibiotics prevent blindness and devastating visual disability. Patients wearing cosmetic lenses are at an increased risk due to lower patient education and the absence of follow-up visits.

Multidrug resistance might be a significant concern in cases of keratitis and corneal ulcer. In the referral centers dealing with corneal ulcers, the initial antibiotic regimens should be changed from time to time to prevent this phenomenon. Resistance to antibiotics such as chloramphenicol, cefazolin, and trimethoprim is very common and these antibiotics should not be considered for empirical treatment. Our outcomes indicate ceftazidime or ciprofloxacin in combination with amikacin is the most effective regimen for the initial treatment of keratitis and corneal ulcers.

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