Original Article

Contact Lens Microbial Keratitis and Prior Topical Steroid Use: A Disaster in the Making?

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Abstract

Introduction: To review the best-corrected visual acuity, ulcer size, microbiological profile and morbidity of contact lens-related microbial keratitis with and without prior topical steroid use. Materials and Methods: Retrospective case review of admitted cases of contact lens-related microbial keratitis in a tertiary hospital. Data pertaining to demographics, pre-admission treatment with or without topical steroids, ulcer size, duration of admission, Gram stain and culture results as well as the final best-corrected visual acuity were recorded. Patients are classified into 3 groups: Group 1 received no treatment prior to presentation, Group 2 received topical antibiotics only from their general practitioners and Group 3 prescribed both topical antibiotics and steroids. Results: Forty-six cases were enrolled in the study, 41.3% had prior topical steroids (all dexamethasone) in combination with antibiotics. None of them had topical steroids alone. Large ulcers were associated with steroid use, odds ratio = 7.74 [95% confidence interval (CI), 1.18-50.56] and positivity of Gram stains odds ratio = 7.74 [95% CI, 1.18-50.56] whereas loss of more than 2 Snellen lines was associated with *Pseudomonas aeruginosa* infection, odds ratios of 21.70 [95% CI,2.09-225.03] and presence of central ulcer, 13.51 [95% CI, 2.33-78.3]. Prior topical steroid use was associated with longer duration of symptoms prior to admission but not duration of stay or surgical intervention. Conclusion: Patients with prior topical combined antibiotics-steroids present slightly later and with larger ulcers. However, the duration of stay, final visual acuity, treatment failure and complication rates were not statistically different from the non-treated group. This might be due to 1) early presentation and therefore early treatment of contact lens-related microbial keratitis and 2) the short duration of use of combined antibiotic-steroid eye drops.

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Introduction

Topical steroid use in cornea ulcers is still a very contentious issue in ophthalmology. A recent review by Wilhelmus found that the use of topical steroids before the diagnosis of bacterial keratitis significantly predisposed eyes with preexisting corneal disease to ulcerative keratitis.[1] Furthermore, once microbial keratitis occurred, prior corticosteroid use significantly increased the odds of antibiotic treatment failure or other infectious complications.[1] A case series reported by Baum and Dabezies[2] suggested that the use of a topical corticosteroid alone with strict guidelines may have a role in the treatment of presumed sterile mid-peripheral corneal infiltrates associated with soft contact lens. This therapeutic option had been feasible because of the ophthalmic expertise present, the availability of diagnostic and laboratory support as well as the presence of stringent clinical guidelines. Even so, 1 of their patients eventually had culture-positive *Pseudomonas* and fortunately, treatment was successful with eventual return to 6/7.5 vision.

Contact lens-related microbial keratitis is the most serious problem of contact lens wear, accounting for 34% of all cornea ulcers admitted to our institution from 1992 to 1993.[3] The prevalence of contact lens use is 9% in Singapore.[4]

In our experience, patients complaining of contact lens-

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related red eyes and treated with topical antibiotic-steroids by general practitioners before presentation to the ophthalmic services are increasingly common. Published clinical practice guidelines for contact lens use state that clinicians should exclude a microbial cause of keratoconjunctivitis and refrain from prescribing steroid eye-drops when a contact lens wearer presents with a red eye. This recommendation was made with level IV evidence (evidence obtained from expert committee reports or opinions and /or clinical experiences of respected authorities).[5]

We undertook this study to examine the impact of prior topical antibiotic-steroid medications prescribed by general practitioners on the outcome of patients admitted to a tertiary institution for contact lens-related microbial keratitis.

Materials and Methods

We examined the case records of all patients admitted for contact lens-related microbial keratitis to the Ophthalmology ward in a tertiary institution in Singapore between 24 May 1999 and 23 May 2001 (24 months).

Contact lens-associated microbial keratitis is defined as cornea epithelial defects associated with infiltrates with a recent history of contact lens use.

Data pertaining to demographics, pre-admission treatment with or without topical steroids by general practitioners, of the length and breadth of ulcers measured using the slit-lamp technique, duration of admission, Gram stain and culture results as well as the final best-corrected visual acuity were recorded.

Patients are classified into 3 groups based on their pre-admission treatment profile in general practice. Group 1 included patients who received no treatment prior to presentation. Group 2 included patients who received topical antibiotics only from their general practitioners and Group 3 patients who were prescribed topical antibiotics and steroids in combination.

Ulcers are considered central if the contact lens-related microbial keratitis affects the visual axis. Peripheral ulcers occurred if they were lateral to the mid-point of an imaginary line between the visual axis and limbus.

The area of ulcer (approximation) was calculated as = length x breadth /mm^2. This area gives an approximation of the area of ulcer to facilitate statistical analysis.

Duration of symptoms was recorded as the duration between the onset of symptoms and presentation at our centre.

Deterioration in visual acuity was calculated using the BCVA in the fellow eye minus the best-corrected visual acuity of the affected eye once the ulcer had re-epithelialised and scarred with the best-corrected visual acuity stable over 2 visits. We assumed that the visual acuity was similar in both eyes before ulceration because pre-disease BCVA were unavailable.

All statistical analyses were performed using a proprietary software package SPSS v10.0 (SPSS, Chicago, IL). Descriptive statistics were used to derive means, standard deviation and distributions of variables. The Kruskal-Wallis test was used for comparing ulcer areas that were non-treated, those treated with antibiotics and those treated with antibiotics-steroids combination. Post hoc Bonferroni tests were performed using Mann-Whitney U test for 2 independent groups. Fisher's Exact test was used to compare data in 2 x 2 contingency tables when one cell had expected count of less than 5. Pearson Chi-square test with 2 degrees of freedom was used to compare treated and non-treated groups in terms of positivity of Gram stains and culture on 3 x 2 contingency tables.

To identify independent predictors of ulcers of areas equal to or greater than 4 mm^2, for differences in BCVA between eyes of more than 2 lines, logistic regression analyses were performed with the best subset variables selection method.

P value of <0.05 was considered statistically significant.

Results

Sixty patients were admitted during the study period, of which 14 patients were excluded because of diagnosis or lack of relevant study data. Four cases were excluded because they had diagnoses other than infective keratitis, i.e., 2 cases of corneal abrasions, 1 case of marginal keratitis and 1 case of non-infective stromal infiltrate. In the remaining 10 patients, there were no historical data with regard to pre-admission treatment by general practitioners and therefore had to be excluded. The final study group comprised 46 (76.7%) patients from the original group.

Table 1 shows the demographical distribution of patients in the study. There are more patients who were untreated (58.7%) than treated. The group comprised Chinese (63%), Malays (28.3%) and Indians (2.2%) and there were gender differences, with a predominance of females (67.4%). The majority of these patients were using monthly disposable contact lenses (58.7%). Interestingly, 1 of the patients was using daily disposable lens and none of the patients were using rigid gas-permeable lenses.

Table 2 shows the variation of antibiotics and steroid treatment prior to presentation at this institution. None of the patients had been treated with topical steroids alone while all those with combination therapy had topical steroids in the form of dexamethasone. Sixty-two per cent of treated patients had topical antibiotic-steroid treatment. Among these, the antibiotic most frequently prescribed was gutt

Table 1. Demographics

	Topical antibiotics alone or antibiotics and steroids in combination
	Total
Race	
Chinese	29
Malays	13
Indians	1
Other races	3
Total	46
Gender	
Male	15
Female	31
Total	46
Laterality	
Right eye	20
Left eye	27
Contact lens	
Daily	1
Weekly	0
Biweekly	7
Monthly	27
Conventional	7
Unknown	4
Total	46

Table 2. Treatment Profile Prior to Presentation

	Combination therapy with topical steroids	
	Yes	No
Antibiotics		
Soframycin	0	1
Chloramphenicol	4	4
Ciprofloxacin	1	1
Gentamicin	0	2
Chloramphenicol + tetracycline	2	0
Neomycin	5	0
Combined polymyxin/tetracycline ointment + natamycin eyedrops	1	0
Topical steroids only	0	0
Total	13	8

Table 3. Ulcer Characteristics

	Treatment with topical drops			Total
	No	Yes		
		Antibiotics alone	Antibiotics with steroids	
Sites of ulcer				
Central	8	2	4	14
Paracentral	13	3	8	24
Peripheral	6	1	0	7
Multifocal	0	0	1	1
Total	27	6	13	46
Area of ulcer (mm^2)	3.97 ± 5.69	4.45 ± 9.15	5.30 ± 4.97	$P = 0.047$*

* Kruskal-Wallis test

Table 4. Microbiology

	Treatment with topical drops			
	No	Yes		
		Antibiotics only	Antibiotics in combination with steroids	
Gram stain				
Negative	16	6	8	
Positive	7	0	3	$P > 0.302$*
Culture				
Positive	14	5	7	
Negative	9	3	4	$P = 0.987$*
Organisms				
Group A beta-haemolytic *Streptococcus spp.*	1			
Bacillus spp.			1	
Klebsiella spp.	1			
Proteus mirabilis	1			
Pseudomonas aeruginosa	8	5	6	
Serratia spp.	2			
Staphylococcus aureus	1			

* Pearson Chi-square test

neomycin, followed by chloramphenicol and chloramphenicol in combination with tetracycline. In the group without steroids, gutt chloramphenicol was the most frequently prescribed antibiotic, followed by gutt gentamicin. Gutt gentamicin 0.3% was used in these cases with inadequate dosing frequency of 3 to 4 times daily.

Table 3 shows the ulcer characteristics. As expected, there were far fewer peripheral ulcers (15.2%) than central ulcers (82.6%). Ulcer sizes were significantly different among the treatment groups. Post hoc Bonferroni tests showed that the antibiotic-steroid treated contact lens-related microbial keratitis group had larger ulcers compared with those without treatment ($P = 0.045$) and those treated with antibiotics alone ($P = 0.022$). There was no significant difference between the untreated group and the group which received antibiotics alone group ($P = 0.355$). There was no relationship between central ulcers and antibiotic-steroid use ($P = 1.0$).

Table 4 shows the microbial profile. Surprisingly, prior topical medication affected neither the Gram stain nor culture results. One patient who developed fungal infection self-discharged from the hospital, against medical advice, just before admission and therefore has no history of prior treatment. This patient was excluded from the study. Otherwise, the antibiotic-steroid treated group did not

Table 5. Morbidity

	Treatment with topical drops			
	No	Yes		
		Antibiotics only	Antibiotics in combination with steroids	
Duration of symptoms	1.6 ± 1.0	2.0 ± 1.2	2.9 ± 1.9	P = 0.031*
Duration of hospitalisation	4.9 ± 2.4	3.8 ± 1.47	5.5 ± 1.6	P = 0.859*
Loss of Snellen lines	0.69 ± 0.88	0.5 ± 0.84	0.5 ± 0.84	P = 0.397*
Surgical intervention			1 anterior lamellar tectonic keratoplasty	

* Kruskal-Wallis test

show an increase in fungal, acanthamoeba or *Pseudomonas* infection. All culture-positive *Pseudomona* infections were sensitive to gentamicin.

There was statistically significant delay in the presentation among patients in the treated groups. However, after controlling for confounding factors with logistic regression, the delay in presentation after the onset of symptoms was not a predictive factor for either loss of Snellen lines or large ulcer size. Figure 1 shows the difference in visual acuity between affected and fellow eyes. The distribution in terms of Snellen lines lost was similar between the non-treated and antibiotic only groups. There is slightly greater but non-significant visual loss in the antibiotic-steroid treated group. There was only 1 case belonging to the antibiotics with steroid group that had surgical intervention. This patient who received prior topical neomycin and dexamethasone treatment, had Gram and culture-positive *P. aeruginosa* ulcer and subsequent anterior lamellar therapeutic keratoplasty for glare and visual problems from a dense anterior stromal scar.

Stepwise logistic regression using ulcer greater than or equal to 4 mm^2 as the dependent variable showed that prior topical antibiotic-steroid use and positivity of Gram stain were significant predictors with odds ratios of 7.74 [95% CI, 1.18-50.56] (P = 0.033) and 7.74 [95% CI, 1.18-50.56] (P = 0.033), respectively. When there were 2 or more Snellen line differences between the eyes, culture positivity for *P. aeruginosa* and presence of a central cornea ulcer were strongly associated with odds ratios of 21.70 [95% CI, 2.09-225.03] (P = 0.004) and 13.51 [95% CI, 2.33-78.31] (P = 0.014).

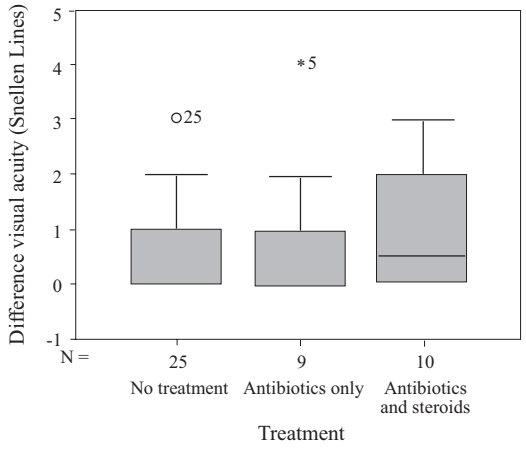

Fig. 1. Difference in visual acuity between affected and fellow eyes.

Discussion

This study shows that in patients with contact lens-related microbial keratitis of a degree of severity that warrants admission to hospital, topical steroids used in conjunction with antibiotics resulted in ulcers larger than 4 mm^2 (odds ratio = 7.74). The loss of Snellen lines was associated with positivity of gram stains, presence of *Pseudomonas* and centrality of ulcer, but not with topical steroid use.

Possible hypotheses to explain our findings of worse ulcers in the antibiotic-steroid group included inadequate dosing of antibiotics, resistance of bacteria to antibiotics, suppression of host local immunity and promotion of penetration of stroma by bacteria such as *Pseudomonas*. Unfortunately, we are unable to determine the possible reasons in this retrospective study due to lack of data in these areas. Other possible hypotheses include: 1) steroids improving symptoms resulting in a delay and subsequent deterioration of ulcer under inadequate antibiotics cover or 2) conversion of a non-infective epithelial defect into contact lens-related microbial keratitis. However, logistic regression analyses found that duration of symptoms was not a significant independent variable, and hypothesis (1) had to be rejected. In any group, the mean time to presentation was very short, being between 1½ to 3 days. It could be because contact lens wearers are younger (mean age, 23 years) and are more likely to present early for treatment of their symptoms rather than allow their conditions to deteriorate to an advanced stage.

Conversion of non-infective epithelial defects into contact lens-related microbial keratitis by topical antibiotic-steroids might be possible. Previous animal studies on topical steroids have shown the adverse effects of steroids on bacterial keratitis, which can enhance stromal growth of *P. aeruginosa* infection.[6-8] Secondly, 46.2% of the antibiotics used in this series were chloramphenicol, which *Pseudomonas* organisms were resistant to. Thirdly, natamycin and neomycin were generally prescribed to be taken 3 to 4 times daily, which was probably inadequate for corneal infection.

Loss of Snellen lines is associated with central ulcers affecting the visual axis and *Pseudomonas* infection. Topical antibiotic-steroids, although associated with larger ulcers, did not seem to influence the visual acuity outcome. This could be due to the fact that the treatment failure rates in this group were very low. All culture-positive *Pseudomonas* infections were sensitive to topical gentamicin, which was the default empirical therapy for contact lens-related microbial keratitis in our centre. Indirect inference to severity using the prolonged duration of hospitalisation as a marker of treatment failure, did not suggest differences across the 3 groups. Only 1 patient in the steroid group has required surgical intervention anterior lamellar tectonic keratoplasty for poor vision due to a central corneal scar. While other measures such as stereoscopic vision or contrast sensitivities might show differences between the groups, these tests were not routine in our cornea clinics for patients with such complaints.

Microbial spectrum was not changed dramatically by the prior use of antibiotics-steroids. There was no increase in the rates of fungal infection or *Pseudomonas*. Neither were the positivity rates of Gram stains nor culture results affected.

It may be argued that some of the infiltrates in our cases may be sterile and may benefit from steroid use, hence masking the deleterious effects of steroids in cases of true contact lens-related microbial keratitis. We agree that this possibility remains but our study lacked the sensitivity of a prospective study and the information required to answer this question. Nevertheless, we actively discourage the use of steroids before diagnosis and even in the context of sterile keratitis, close and careful monitoring in an ophthalmic setting is warranted before steroid treatment is instituted.

One particular concern is that 28.3% of these patients were Malays even after adjusting for age and gender. This figure is high, considering that Malays comprise 13.8% of the population[9] and 12.3% of contact lens wearers in Singapore are Malays.[4] The likelihood of selection bias is minimal as this institution serves the community nationwide. In spite of the proportionately high rate of affliction for this ethnic group, they do not seem to have worse ulcers or poorer visual outcome. It may be worthwhile to increase the awareness of contact lens management within this ethnic group.

Our study is limited in the sense that it is a retrospective, non-randomised study. There are potential confounding factors in our study, such as the initiation of antibiotic-steroids in patients who have worse symptoms, poor patient compliance with regard to medication, variations in prescribing habits and unknown duration of steroid use. Besides, we were unsure whether contact lens-related microbial keratitis developed before or after the start of topical antibiotic-steroids. Consequently, probable duration of ulcers could only be estimated from the duration of symptoms.

It is imperative that clinicians should work closely with general practitioners in the management of contact lens-related microbial keratitis. Also, since the majority of contact lens-related microbial keratitis is caused by *P. aeruginosa*, it would be prudent for general practitioners to use ciprofloxacin rather than chloramphenicol as the first-line antibiotic.

In conclusion, patients with prior topical antibiotic-steroids present slightly later and with larger ulcers. The duration of stay, final visual acuity, treatment failure and complication rates were not statistically different from those of the non-treated group. This might be due to 1) early presentation and therefore early treatment of contact lens-related microbial keratitis and 2) the short duration of use of combined antibiotics-steroid eye drops.

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