Management of bacterial corneal ulcers

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SUMMARY A prospective microbiological study of 48 patients with corneal ulcers due to bacterial infection was performed. Positive cultures of corneal ulcer samples were obtained in 60% of all patients; about half of these patients had received antimicrobial treatment prior to sampling. A relatively high incidence of *Staphylococcus epidermidis* was isolated from ulcer patients (27%) compared with normal controls (10%). Gram stains of ulcer samples were positive for organisms in only 27% of all patients and were not considered useful in determining initial therapy in this series. We concluded that treatment should be started with a broad combination of antibiotics while awaiting the culture results.

Despite the easy access of the cornea to therapeutic agents the treatment of bacterial corneal ulcers remains a problem. There are basically two approaches to the management. The specific therapy advocated by Jones¹ is most widely accepted and is based on the examination of corneal scrapings with culture identification of the offending organism and treatment of the ulcer according to its antibiotic sensitivity. Alternatively the broad therapy developed by Baum² is based on the prevalence of organisms known to produce disease in a particular geographic location. A broader treatment regimen according to the known sensitivities of the most likely organisms is given.

Both approaches require a knowledge of the causative organisms and their sensitivities. This paper presents the findings of a microbiological study of patients with bacterial corneal ulcers referred to Groote Schuur Hospital for treatment. Peripheral staphylococcal ulcers have been specifically excluded from the study.

Patients and methods

During the period January 1983 to March 1984, 48 patients were seen at Groote Schuur Hospital with clinically diagnosed bacterial corneal ulcers. All cases of uninfected erosions, viral keratitis, fungal keratitis, and peripheral staphylococcal infection have been excluded from this study. Patients' ages ranged

between 8 and 80 years with an average of 50 years; 69% were males and 31% females.

On admission of the patients to hospital corneal samples were taken for Gram stain and culture. The cornea was anaesthetised with 0.4% oxybuprocaine solution without preservative (Minims Benoxinate). In each case samples were taken from the base and leading edge of the ulcer by means of sterile calcium alginate swabs,³ care being taken to avoid touching the conjunctiva and lids. The material was spread over a localised area on precleaned glass slides for immediate Gram stain and microscopic examination. Further samples were taken for direct inoculation into cooked meat medium, boiled blood agar, and Sabouraud's agar for culture identification of organisms. Corneal and conjunctival swabs were taken for similar Gram stain and culture from 39 control patients with clinically uninfected eyes admitted for routine surgery such as lens extraction and squint correction.

Our treatment regimen followed that advocated by other authors.^{1,3} The initial treatment was based on the results of the corneal smears. All patients received 1% atropine drops twice daily. Gram-positive cocci were treated with subconjunctival cephamandole and hourly topical 10% cephamandole drops, and Gram-negative bacilli were treated with subconjunctival gentamicin and hourly topical 3% gentamicin drops. If no organism was identified both cephamandole and gentamicin were used. The subsequent management of all ulcers was determined by the culture and sensitivity results as well as the clinical response to treatment.

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Results

GRAM STAIN RESULTS

Pus cells were present on the smears taken from 38 patients (79%). However, in all the remaining patients who showed no pus cells on the smear there was clinical evidence of infective keratitis, with a frank hypopyon in all but one of these cases. Organisms were identified on the smears taken from 13 patients (27%), seven patients showing Gram-positive cocci and six Gram-negative bacilli.

CULTURE RESULTS

Positive corneal cultures were obtained from 29 patients (60%). Gram-positive cocci were most commonly isolated, but Gram-negative bacilli and mixed bacterial ulcers were also identified (Table 1). Fifteen of these patients had received antibiotic therapy (chloramphenicol 14; neosporin 1) for a variable period before being referred to us and, therefore, before their corneal smears were taken for culture.

Of the 19 patients with negative corneal cultures eight had received antimicrobial therapy before being referred to us and culturing (chloramphenicol

Table 1 Organisms cultured from corneal ulcers

Organism	Number of isolates	Prior therapy*
Gram-positive cocci:	20	12
<i>Staph. aureus</i>	4	2
<i>Staph. epidermidis</i>	9	6
<i>Str. pneumoniae</i>	6	3
<i>Str. viridans</i>	1	1
Gram-negative bacilli:	5	1
<i>Pseudomonas aeruginosa</i>	3	1
<i>Moraxella</i> species	1	—
<i>Haemophilus influenzae</i>	1	—
Mixed infections:	4	2
<i>Staph. epidermidis</i> /diphtheroids	4	2

*See text for details.

Table 2 Gram stain and culture correlation

Gram stain	Culture	No. patients
Gram and culture correspond (8 patients)		
Gram-positive cocci:	<i>Str. pneumoniae</i>	2
	<i>Staph. epidermidis</i>	2
Gram-negative bacilli:	<i>Pseudomonas aeruginosa</i>	2
	<i>Moraxella</i> species	1
	<i>Haemophilus influenzae</i>	1
Gram and culture different (5 patients)		
Gram-positive cocci:	No growth	3
Gram-negative bacilli:	No growth	1
	<i>Str. viridans</i>	1

Table 3 Organisms isolated from 39 control patients

Organism	Number of isolates	
	Conjunctiva (%)	Cornea (%)
No organisms	33	87
<i>Staph. epidermidis</i>	49	10
<i>Staph. aureus</i>	13	0
<i>Bacillus</i> species	5	3

5; framycetin 1; tobramycin 1; sulphacetamide 1).

Of the 13 patients with positive Gram stains organisms were cultured from nine; eight of these were appropriate to the Gram stain and the other one was different from what the Gram stain showed (Table 2). From the remaining four patients no organisms were cultured.

Although we cultured organisms from 60% of patients, not all positive cultures were necessarily significant. There was a relatively high incidence of *Staphylococcus epidermidis* (27% of all patients), which is a normal resident of conjunctiva and lids.⁴ To clarify the role of *Staph. epidermidis* we took corneal and conjunctival swabs from 39 control patients with clinically uninfected eyes admitted for routine surgery.

NORMAL CONTROLS

Organisms were isolated from 67% of conjunctival swabs but only 13% of corneal swabs taken from the same eye of 39 control patients (Table 3). There was a high incidence of *Staph. epidermidis* cultured from the conjunctival swabs, thus confirming its residential status in the conjunctiva. Most of the corneal organisms cultured were also *Staph. epidermidis*; in all cases the organisms cultured from the corneal swabs were also found in the conjunctival cultures, indicating that these organisms were present in the pre-corneal tear film.

Discussion

The successful management of bacterial corneal ulcers is based on prompt identification of the causative organism and effective treatment with an appropriate antibiotic.^{1,5} Unfortunately the Gram stain and culture results are not always positive. We cultured organisms from 60% of patients with corneal ulcers, and this compares favourably with the results of other authors, who have reported incidences of positive cultures ranging between 53% and 73%.⁴⁻⁸

A number of factors may influence the culture results. Usually only a small amount of material is available, giving a light growth of organisms. Topical anaesthetic agents are known to have antimicrobial

activity and their use may lead to false negative culture results.⁸ We instilled preservative-free Minims Benoxinate immediately before taking samples for culture, as it does not interfere significantly with the isolation of organisms from corneas.⁸ This made the sampling procedure more comfortable for our patients, enabling us to obtain adequate samples without touching the lids or conjunctiva.

Treatment of ulcers with antibiotics prior to corneal culturing may also reduce the number of positive results. Almost half (23 patients) of all our corneal ulcer patients received topical antibiotics before smears were taken for culture. However, it is significant that about half of the patients with positive cultures had been treated with antibiotics prior to culturing. Thus previous treatment does not necessarily preclude positive culture results and should not be a reason for avoiding sampling.

In this study we have followed the type of regimen advocated by Jones¹ in which the initial therapy was based on the results of the Gram stain and treatment was subsequently adjusted according to the culture and sensitivity results. Our Gram stain results were disappointing because organisms were identified in only 27% of all patients, and subsequent culture confirmed the identity of these organisms in only 57% of these patients. The Gram stain was therefore not very useful in determining the appropriate initial therapy in our series. In one patient a different organism was cultured. On the Jones regimen this patient received inappropriate medication until the time that the culture report was available. Since it often takes 48 hours before the culture results are known, we now prefer to ignore the Gram stain and start treatment with a broader combination regimen while awaiting the culture results.⁵ Treatment may subsequently be modified according to the sensitivity of the organism as well as the patient's response to treatment.

A relatively high incidence of *Staph. epidermidis* was isolated from our corneal ulcer patients (27%). This organism is a normal resident of conjunctiva and lids,⁴ and its role in ocular disease has been the subject of much controversy recently.^{7,9,10} It is known to be pathogenic in some immunologically compromised patients.¹¹⁻¹³ We found that in all normal control cases with positive corneal cultures the same organism was isolated from the conjunctival cultures from the same eye. These organisms were therefore present in the precorneal tear film and could either colonise or contaminate an area of corneal ulceration

sufficiently to be detected on the corneal culture.¹ Unfortunately this does not answer the question of the pathogenicity of *Staph. epidermidis*. However, it may be pertinent that a higher incidence of *Staph. epidermidis* was cultured from the patients with corneal ulcers (27%) than from the normal controls (10%). This suggests that some of these ulcers were due to exogenous *Staph. epidermidis* or alternatively that patients having this organism resident are more prone to infection. Mahajan *et al.*^{7,12} have shown that approximately one-third of isolates of *Staph. epidermidis* taken from various types of ocular infections showed dermonecrotic activity and were therefore regarded as pathogenic. Although *Staph. epidermidis* may not be of importance in all ulcers, it cannot be disregarded, and it would seem prudent to treat such an infection actively.

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