Author's response to reviews

Title: Clinical And Microbiological Profile Of Infectious Keratitis In Children

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Author's response to reviews: see over
Dear Professor Dick:

On behalf of all authors I would like to submit for your revision the manuscript entitled "CLINICAL AND MICROBIOLOGICAL PROFILE OF INFECTIOUS KERATITIS IN CHILDREN" with all revisions requested by the reviewers. A point by point description of all modification is included at the end of this letter. Every question was answered and the data demanded by the reviewers is included.

Kind regards,

Patricia Chirinos Saldaña & Enrique Graue Hernández
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Reviewer 1: Rasik B Vajpayee

1. The conclusions section of the abstract does not match the results section of the abstract. Please revise accordingly.

We revised and modified the abstract to match results and conclusions. In the conclusion, only factors evaluated in the study were considered.

Results: Forty-one eyes of 41 patients. Mean age was 8.7 years. Time between the onset of symptoms and ophthalmological examination was 12.7 days. Predisposing factors were found in 78%; ocular trauma was the most common (25%). Mean corrected distance visual acuity at admission was logMAR 1.49 ± 1.15 and at discharge logMAR 0.76 ± 0.64. Positivity of cultures was 34%. Gram-positive bacteria were isolated in 78.5%; *Staphylococcus epidermidis* (28.6%) was the most common microorganism.

Conclusions: Our study emphasizes the importance of a prompt diagnosis and treatment of infectious corneal ulcers in children. Trauma and contact lenses were the main predisposing factors. Gram-positive organisms were isolated in the vast majority of cases and visual outcomes are usually poor.

2. How were the patients identified for retrospective analysis?

A search was performed within the database of the electronic medical records at our institution. The terms “infectious keratitis”, ”corneal ulcer”, “bacterial keratitis”, “mycotic keratitis”, “viral keratitis” were used. A filter using the birth date and the date of first appointment at the cornea clinic was used further select the cases. A manual revision of all records to check that the files selected fullfilled the inclusion criteria was then performed.
3. Was a corneal scraping performed or conjunctival swabbing? Please add details.

In all patients, corneal scrapings were obtained, smears were prepared for standard microbiologic evaluation including Gram and Giemsa stains, The sample was sowed in Columbia agar + 5% sheep, chocolate agar + PolyViteX (PVX) and Brain-Heart Infusion (BHI), those were incubated at 37°C and 5% CO; and Sabouraud dextrose agar, which was incubated at 28°C and 5% CO.

4. The authors can briefly discuss other etiologies for microbial keratitis in children in the developing world such as poor nutrition and poor immunization profile. Please refer to the publication


The text discusses and cites the referred article. In the article by Jhanji et al, Immunization status was associated with malnutrition but its effect on corneal ulceration was not assessed.

5. How many cases required surgical intervention? What was the nature of surgical intervention?

Perforation occurred in a single case and was treated with tectonic keratoplasty
1. The manuscript needs a description of the microbiology methods, treatment protocols, what were the criteria for a positive culture. 34% might be a low culture proven rate or as expected based on the methods.

Microbiology Workup

In all patients, corneal scrapings were obtained, smears were prepared for standard microbiologic evaluation including Gram and Giemsa stains. The sample was sowed in Columbia agar + 5% sheep, chocolate agar + PolyViteX (PVX) and Brain-Heart Infusion (BHI), those were incubated at 37°C and 5% CO; and Sabouraud dextrose agar, which was incubated at 28°C and 5% CO. The bacteria were identified using the Vitek 2 Compact system (bioMérieux, France) with GP-test Vitek card. The drug sensitivity was determined by the Kirby-Bauer method using the following antibiotic discs: polymyxin, oxacillin, neomycin, sulfamethoxazole, vancomycin, gentamicin, ciprofloxacin, ofloxacin, cephalothin, cephazolin and ceftazidime and according to Clinical and Laboratory Standards Institute guidelines [9]. Criteria for culture positivity were growth of the organism at the site of inoculation on two or more solid phase cultures, or growth at the site of inoculation on one solid phase media of an organism consistent with microscopy, or confluent growth on one media.

As mentioned previously initial medical therapy was based on fourth generation fluoroquinolones and modified according to clinical response or antibiogram. In 26 patients (63.4%) this therapeutic regimen remained (0.5% moxifloxacin or 0.3% gatifloxacin); 6 (14.6%) were switched to macrolides (0.5% erythromycin); 5 (12.2%) to third generation cephalosporins (5% ceftazidime); 3 (7.3%) to third generation fluoroquinolones (0.3% ciprofloxacin) and 1 (2.4%) to topical 0.15% amphotericin B together with 1% natamycin and systemic oral itraconazole.
2. Reporting of significant figures age & days to presentation don't need reporting to 2 decimal places.

The text was modified as suggested.

3. There is a strange selection of the denominator in several of the rates presented. The rates for different organisms for example would generally be expressed as a proportion of the positive cultures rather than a fraction of the total sampled. This might make it easier to compare with other literature. Similarly for the frequency of different risk factors.

The text was modified as suggested.

4. In tables 1 and 2 the numbers of trauma cases don’t match 8 in table 1 and 7 in table 2. Table 2 could probably be incorporated into the text.

The text was revised as suggested. There were 8 cases of ocular trauma. We eliminated table 2 and incorporated the data into the text.

Predisposing factors were identified in 78% of cases, with 2 or more factors occurring in 26%. The most common predisposing factor was ocular trauma (25%), followed by wearing contact lenses and prolonged steroid treatment (Table 1). In cases associated with ocular trauma, pencils were the most common cause (10.6%); other was associated with fireworks, cat scratch, rope, soil and toys.

5. There is inconsistency in the reporting of results in the text on page 5 and table 3. For example the description of the gram positive isolates is confusing: table shows 10 and text shows 9. The text describes 2 gram negative bacilli as P.aeruginosa but the table describes 2 P.aeruginosa and 2 further gram negative...
bacilli. I would suggest referring to the table only and avoiding duplication or inconsistency. What were the additional gram negative bacteria, these need reporting to the species level.

We corrected the inconsistency in table 3 (now table 2). There are 11 gram positive bacteria and two gram negative bacilli (Pseudomonas aeruginosa).

6. Page 5 re antibiotic sensitivity testing, should this read Staphylococcus spp. Not sp. or are the authors referring to either S.aureus or S.epidermidis. Please clarify.

We referred to both S. aureus and S. epidermidis, therefore we replaced sp. by spp.

7. Could table 3 also incorporate the risk factors associated with the organism recovery

No significant association between risk factors and culture positivity was encountered.

8. There is mention of prior antibiotic treatment in a proportion of cases, but the care pathway is not discussed. This would seem important in reducing the morbidity associated with the disease. Also it is not clear from the methods which of the possible reasons for a low culture proven rate would be likely in this study, for example how were samples taken.

We added the antibiotic treatment instaured:

Initial medical treatment was based on fourth-generation fluoroquinolones monotherapy and modified in accordance with clinical response, culture and antibiotic susceptibility results.

As mentioned previously initial medical therapy was based on fourth generation fluoroquinolones and modified according to clinical response or
antibiogram. In 26 patients (63.4%) this therapeutic regimen remained (0.5% moxifloxacin or 0.3% gatifloxacin); 6 (14.6%) were switched to macrolides (0.5% erythromycin); 5 (12.2%) to third generation cephalosporins (5% ceftazidime); 3 (7.3%) to third generation fluoroquinolones (0.3% ciprofloxacin) and 1 (2.4%) to topical 0.15% amphotericin B together with 1% natamycin and systemic oral itraconazole.

Self-prescribed antibiotic, microorganisms with slow growth on culture media, viral causes of keratitis, improper corneal sampling, and the inherent difficulty in getting corneal samples from pediatric patients may account for the low positivity rate observed in our study.

9. Page 6, hypoxia in adult contact lens wearers is unproven as a risk factor for microbial keratitis.

We modified in the text: Interactions between contact lens and ocular surface instead of hipoxia and cited 2 articles.


10. Were the contact lens wearers using lenses for orthokeratology?

None of contact lens wearers used orthokeratology lens.
11. It is difficult to conclude changes in sensitivity over time with so few culture proven cases.

   We agree, and eliminate de last paragraph about gentamicin.