Trimethoprim-polymyxin B sulphate ophthalmic ointment in the treatment of bacterial conjunctivitis: a double-blind study versus chloramphenicol ophthalmic ointment

W. Behrens-Baumann, M.D.,
C. D. Quentin,* M.D.,
J. R. Gibson,** M.B., Ch.B.,
I. G. Calthrop,** B.Sc.,
S. G. Harvey,** B.Sc.,
and
K. Booth,** B.Sc., M.Sc.

Augenklinik and Poliklinik, Georg-August-Universität, Göttingen.
*Zentrum Augenheilkunde and Hals-Nasen-Ohrverheilkunde, Abteilung Augenheilkunde, Götingen, West Germany.
and **The Wellcome Research Laboratories, Beckenham, England

Summary

Forty-two patients with a clinical diagnosis of bacterial conjunctivitis were enrolled in a randomized, double-blind trial. Patients were treated with either trimethoprim-polymyxin B sulphate or chloramphenicol ophthalmic ointments 4-times a day for 7 days. Analysis of clinical evaluation data showed that both treatments were effective and well tolerated, and that there were no statistically significant differences between them with regard to eradication of organisms or clinical improvement.

Key words: Trimethoprim – polymyxin B – chloramphenicol – ophthalmic ointments – conjunctivitis, bacterial

Introduction

Trimethoprim is a broad-spectrum antibacterial agent with activity against both Gram-positive and Gram-negative organisms. Polymyxin B sulphate has bactericidal activity against a wide range of Gram-negative organisms, including Pseudomonas aeruginosa, and has been widely used, especially as a topical therapy.

The rationale behind the combination of trimethoprim and polymyxin B sulphate for topical treatment of bacterial infections of the eye is as follows: (i) the combination provides a broad spectrum of potent antibacterial activity which surpasses that of the individual agents; such a spectrum of activity is particularly useful as it is common practice for treatment to be prescribed prior...
to determination of the causative agent; (ii) the combination has been shown to be synergistic or additive in action against a range of micro-organisms;13 (iii) both drugs have a low sensitizing potential, with polymyxin B sulphate having been used for many years as a topical agent with remarkably few reports of local allergic hypersensitivity,6 and trimethoprim exhibiting a 0% sensitization rate in the guinea-pig maximization test (Dayan, A. D., unpublished data); and (iv) the activity against *Pseudomonas* species provided by polymyxin B sulphate is useful in view of the potentially serious sequelae of ophthalmic infection by this group of organisms.

We report here the results of a trial comparing trimethoprim-polymyxin B sulphate ophthalmic ointment with chloramphenicol ophthalmic ointment, a widely used antibacterial agent,12 in the treatment of bacterial conjunctivitis.

**Patients and methods**

Patients with a clinical diagnosis of bacterial conjunctivitis, for whom informed consent had been obtained, were entered into the trial. The study was double-blind and parallel in design, with patients randomly allocated to receive trimethoprim-polymyxin B sulphate ("Polytrim") or chloramphenicol ophthalmic ointments. Trimethoprim and polymyxin B sulphate were present at concentrations of 5 mg/g and 10,000 units/g, respectively; chloramphenicol was present at a concentration of 10 mg/g. The dosage regimen was 4 daily applications of ointment to the lower conjunctival sac for 7 days. Unilateral and bilateral infections were considered suitable for treatment; the same treatment was used for both eyes in the case of bilateral infections.

Patients were excluded from the study if they had a known previous allergic hypersensitivity to any of the components of the test medications, if they required concurrent treatment with systemic or topical corticosteroids, antibiotics or antihistamines, or had received systemic or topical antibiotics within 72 hours prior to entry into the study. Patients who had concomitant fungal, viral or tuberculous eye infections or who had contracted more than 6 bacterial eye infections during the previous year were also excluded.

The criteria used to diagnose bacterial conjunctivitis depended on signs and symptoms outlined in Table 1, which were graded according to a scale of 0 to 3, where 0 = none, 1 = mild, 2 = moderate and 3 = severe.

The patients were assessed clinically at the initial visit and again 4 and 10 days after the start of the therapy. In order to confirm the diagnosis of bacterial conjunctivitis, swabs were taken pre-treatment from the lower conjunctival sac. Treatment was commenced prior to receiving the result of the bacteriological swab. A further swab was taken on the patient's final visit.

**Results**

Forty-two patients, (23 males and 18 females) aged between 4 and 72 years (mean age 35.2 ± 4 years), were enrolled in the trial. (Details for sex and age

*trade mark, Wellcome
for 1 patient were not recorded). Twenty-two patients received trimethoprim-polymyxin B sulphate ophthalmic ointment, and 20 patients received chloramphenicol ophthalmic ointment. Data from 41 patients proved to be evaluable at the first follow-up assessment, and 34 patients at the final follow-up assessment.

The results of the clinical evaluation of the patients are summarized in Figure 1 and Table II.

**Figure 1. Mean severity rating scores before, during and after treatment in the two groups**

![Mean severity rating scores](image)

**Table II. Details of patients with given percentage reductions in initial scores for combined symptoms and signs at the final assessment in the two groups: number (%) of patients**

<table>
<thead>
<tr>
<th>Reduction (%) in initial scores</th>
<th>Trimethoprim-polymyxin B sulphate (n=17)</th>
<th>Chloramphenicol (n=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100%</td>
<td>11 (65)</td>
<td>9 (53)</td>
</tr>
<tr>
<td>90% or more</td>
<td>15 (88)</td>
<td>12 (71)</td>
</tr>
<tr>
<td>75% or more</td>
<td>16 (94)</td>
<td>16 (94)</td>
</tr>
<tr>
<td>50% or more</td>
<td>17 (100)</td>
<td>16 (94)</td>
</tr>
</tbody>
</table>

Note: there was no significant difference between groups
Trimethoprim-polymyxin B sulphate ophthalmic ointment in the treatment of bacterial conjunctivitis: a double-blind study versus chloramphenicol ophthalmic ointment

Figure 1 shows the mean scores for combined symptoms, for combined signs, and for combined symptoms and signs as assessed by the investigator before, during and after treatment; Table II shows the proportion of patients with 100%, 90% or greater, 75% or greater, and 50% or greater reduction in their initial scores for combined signs and symptoms at the final assessment. There were no statistically significant differences between the treatment groups (p>0.1, Fisher's exact test).

The bacteriological results are shown in Table III. The strike rate for positive bacterial cultures was good, with 55% of patients having a growth of pathogens or potential pathogens from the pre-treatment swab.

Table III. Results of bacterial cultures before and after treatment: number of isolates

<table>
<thead>
<tr>
<th>Organism</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Trimethoprim-polymyxin B</td>
<td>Chloramphenicol</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Staphylococcus epidermidis</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>(albus)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serratia marcescens</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: this Table shows the range of bacteria isolated during the study, but it does not in all cases directly relate pre-treatment to post-treatment culture results for individual patients.

It will be seen from Table III that Staphylococcus epidermidis was the most common organism cultured during this study; this finding is not unexpected. It should be borne in mind that whilst this organism is traditionally regarded as being non-pathogenic, it would appear that it may be pathogenic in the eye and elsewhere under certain circumstances.

Adverse events

Three (7%) patients reported adverse events during the study period, all of whom were in the trimethoprim-polymyxin B sulphate group: 1 patient experienced stinging/burning, 1 increased transient grittiness and conjunctival hyperaemia and 1 periorbital oedema. The latter 2 patients withdrew before completion of the trial.

Discussion

The results of this study indicate that both trimethoprim-polymyxin B sulphate and chloramphenicol ophthalmic ointments were effective in reducing the clinical signs and symptoms of bacterial conjunctivitis. There were no statistically significant differences between the two preparations. These results are compatible with those obtained in previous studies in which trimethoprim-polymyxin B sulphate ophthalmic solution was consistently shown to be at least as effective as solutions containing chloramphenicol, and another widely used combination, neomycin-
polymyxin B-gramicidin in the treatment of bacterial conjunctivitis. In fact, in one study, trimethoprim-polymyxin B sulphate ophthalmic solution was found to be significantly superior to chloramphenicol ophthalmic solution.

The data obtained in this preliminary study using ophthalmic ointments, when considered alongside published data concerning the respective ophthalmic solutions, indicate that the trimethoprim-polymyxin B sulphate combination represents a good alternative to chloramphenicol in the treatment of bacterial conjunctivitis.

Acknowledgement

The trial medications were supplied by The Wellcome Foundation Limited, Dartford, Kent, U.K.

References