Results of a Survey of Children with Acute Bacterial Conjunctivitis Treated with Trimethoprim-Polymyxin B Ophthalmic Solution

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ABSTRACT

Acute conjunctivitis, one of the most frequently seen eye diseases in infants and children, is associated with a shorter duration of clinical disease when antimicrobial agents are used. Although viruses often are implicated as causative agents, Haemophilus influenzae and Streptococcus pneumoniae are the most commonly isolated bacterial pathogens. Empiric therapy of acute conjunctivitis therefore should include agents with both gram-positive and gram-negative antimicrobial activity. Trimethoprim-polymyxin B is a broad-spectrum antimicrobial agent available as an ophthalmic solution. We conducted a patient outcomes study to evaluate the subjective response to treatment with trimethoprim-polymyxin B of children with presumed acute bacterial conjunctivitis. Questionnaires were distributed to more than 100 pediatricians who assessed outcome measures in 472 children with acute bacterial conjunctivitis for whom they prescribed trimethoprim-polymyxin B. The parameters evaluated were clinical outcome, overall efficacy, and comfort provided by the medication regimen. The physicians reported that 95% of the infected eyes were cured or improved within 7 days. In addition, the overall efficacy of trimethoprim-polymyxin B was rated as excellent or good in 76% and 20% of cases, respectively. With regard to patient comfort, patients or their caregivers reported that patients were very comfortable or moderately comfortable in 62% and 27% of cases, respectively. Four adverse events were reported; all were transient and of mild-to-moderate intensity. The survey results support clinical research findings on the comparative efficacy and safety of trimethoprim-polymyxin B ophthalmic solution compared with other ophthalmic antimicro-
bial agents. The pediatricians in our survey who prescribed trimethoprim-polymyxin B ophthalmic solution for children with presumed acute bacterial conjunctivitis reported that this medication was effective and well tolerated.

INTRODUCTION

Although ocular infections in the pediatric population can be serious, in many cases they are self-limited. One of the most frequently seen eye diseases in children is acute conjunctivitis. Treatment with systemic or topical antimicrobial agents results in a shorter duration of clinical disease and is considered the standard of care.

Treatment of acute conjunctivitis in infants and children is usually empiric, based on coverage of the most likely causative pathogens. In a study of 99 children and adolescents aged 1 month to 18 years, Gigliotti et al found that Haemophilus influenzae, Streptococcus pneumoniae, and adenovirus were the most commonly isolated pathogens. In neonatal conjunctivitis (ophthalmia neonatorum), causative agents can be chemical, chlamydial, or bacterial, particularly Neisseria gonorrhoeae.

In contrast to acute disease, chronic conjunctivitis is not considered a self-limited condition and can lead to complications if not treated. Indeed, sometimes a more serious underlying condition (eg, uveitis) may appear to be a cause of chronic conjunctivitis. Chronic conjunctivitis commonly is of bacterial origin and is much less frequently caused by allergens, chlamydia, viruses, or chemical injury.

Empiric therapy for acute conjunctivitis should include agents with both gram-positive and gram-negative antimicrobial activity. One ophthalmic antimicrobial agent that meets this criterion is trimethoprim-polymyxin B. The objective of our recent patient outcomes study was to evaluate the subjective response to treatment with trimethoprim-polymyxin B of children with presumed acute bacterial conjunctivitis.

MATERIALS AND METHODS

Patient outcomes study questionnaires were distributed to more than 100 pediatricians throughout the United States. Pediatricians were asked to assess outcome measures in children with acute conjunctivitis for whom they prescribed trimethoprim-polymyxin B. The parameters included grading the severity of the bacterial conjunctivitis at baseline and assessing the clinical outcome, overall efficacy, and comfort provided by the treatment regimen.

All completed questionnaires were compiled and tabulated in a computerized database by an independent research group (Health Serve, Newport Beach, California).

RESULTS

A total of 103 physicians completed questionnaires on 472 patients; however, not all questionnaires were complete. Seventy-eight (21%) of 373 patients were younger than age 1 year, 142 (38%) were aged 1 to 5 years, 108 (29%) were aged 5 to 10 years, and 45 (12%) were older than age 10 years.

At baseline, 32% of patients had mild cases, 59% had moderate cases, and 9% of patients had severe cases of acute bacterial conjunctivitis. The physicians reported that 85% of the infected eyes were

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cured and 10% were improved within 7 days (Figure 1). In the physicians’ ranking of overall efficacy, good results were obtained in 20% of patients and excellent results in 76% of patients (Figure 2). With regard to patient comfort, patients or their caregivers reported that patients were very comfortable or moderately comfortable in 62% and 27% of cases, respectively.

Four adverse events were reported, all of which were transient and of mild-to-moderate severity. The adverse events were burning and watering of eyes (1 patient), redness (1 patient), increased drainage requiring a change of medication (1 patient), and mild stinging on instillation (1 patient).

DISCUSSION AND CONCLUSION

As outlined by Lohr,\(^5\) the criteria for developing a treatment strategy for acute conjunctivitis in infants and children is similar to that used for other infectious diseases. This includes identifying the specific infectious agent, when possible; providing subjective and objective clinical improvement; eradicating the infectious agent, preventing recurrences, and decreasing the likelihood of contagion; and avoiding adverse effects. In addition, to enhance compliance, the prescribed medication must be acceptable to patients and parents or caregivers and be reasonably priced.
The results of investigations by Gigliotti et al[6] and Weiss et al[8] suggest that bacteria and viruses cause conjunctivitis in children in 85% to 90% of cases. *H influenzae* and *S pneumoniae* are the most frequently recovered bacteria and adenovirus the most frequently isolated virus. The exception to this prevalence is in the neonatal period during which *Chlamydia trachomatis* is the most common causative agent of acute conjunctivitis.1,2,6 Other gram-negative pathogens associated with acute conjunctivitis in children include *Moraxella catarrhalis*, *Neisseria* species, other *Haemophilus* species, and *Pseudomonas aeruginosa*. The roles of *Staphylococcus aureus* and *Staphylococcus epidermidis* are not clear because both these organisms are present in the normal flora of the eye and have been isolated as pathogens. More rarely, other viruses (including herpes simplex) and fungal organisms are the causative agents of acute conjunctivitis.

Using clinical clues to help determine the cause of acute conjunctivitis may or may not be helpful. Although bacterial conjunctivitis is more likely than viral conjunctivitis to be bilateral and associated with purulent exudate, in the Gigliotti et al[6] series, children with viral conjunctivitis had bilateral infection with purulent exudate in more than 35% of cases. There was an association of *H influenzae* with concurrent otitis media and of adenovirus with pharyngitis, but these relationships were not exclusive and using them may mislead the clinician.
The results of Gram stains, Giemsa stains, or culture and sensitivity tests often are unavailable at the start of therapy in children with acute conjunctivitis. Therefore, treatment usually is empiric, with antibiotic selection based on coverage of both gram-positive and gram-negative pathogens. There are currently no effective treatments for adenovirus. In addition, these laboratory tests often are not performed in cases of acute conjunctivitis in otherwise healthy children; exceptions include children in whom a trial of antimicrobial therapy has failed and those with severe ocular inflammation. Laboratory tests also add considerable cost, both in time and money, to a course of treatment.

Antimicrobial agents with activity against gram-positive and gram-negative organisms and available in an ophthalmic dosage form include trimethoprim-polymyxin B, bacitracin-polymyxin, chloramphenicol, sulfacetamide, tetracyclines, erythromycin, ciprofloxacin, norfloxacin, ofloxacin, neomycin, gentamicin, and tobramycin. In considering the relative utility of these agents in children, chloramphenicol is very effective in this setting, but its well-known association with bone marrow toxicity makes it a second-line choice behind safer drugs such as trimethoprim-polymyxin B and bacitracin-polymyxin. Sulfacetamide is effective and available as a solution or ointment. Its main drawbacks are a high incidence of stinging and burning on instillation and hypersensitivity reactions. The tetracyclines are not recommended because of the risk of permanent discoloration of teeth. Erythromycin is not a typical choice in children with acute conjunctivitis; although it has excellent in vitro activity against S pneumoniae, it is much less effective against H influenzae. The fluoroquinolones (ciprofloxacin, norfloxacin, and ofloxacin) are potent, broad-spectrum agents with proven efficacy in serious infections, such as corneal ulcers. The aminoglycosides also are potent, broad-spectrum agents. Neomycin often causes hypersensitivity or allergic reactions. Gentamicin and tobramycin may cause epithelial toxicity and corneal ulceration with long-term use and promote the development of resistant organisms; these agents should be reserved for treating serious infections.

Products such as trimethoprim-polymyxin B and bacitracin-polymyxin combinations are frequently recommended. Both are effective against the common bacterial pathogens isolated in children with acute conjunctivitis. Trimethoprim-polymyxin B has the advantage of being available in solution, as compared with ointment, which is easier for parents to use in infants and is preferred by older children. Bacitracin-polymyxin products are available in ointment formulations only.

Acute conjunctivitis in children was thought to be primarily of viral origin until Gigliotti et al published their 1981 review demonstrating otherwise. There was therefore not much interest in using topical agents with antibacterial activity until the 1980s when a series of studies were published that evaluated different agents. Systemic antimicrobial agents are usually used when conjunctivitis is concurrent with pharyngitis or otitis media.

In 1984, Gigliotti et al published a study comparing polymyxin-bacitracin ophthalmic ointment and placebo in 102 children and adolescents aged 1 month to 18 years with acute conjunctivitis. There was a statistically significant difference at
days 3 to 5 between active drug and placebo for the outcome of clinical cure, as measured by lid edema, conjunctival erythema, subconjunctival hemorrhage, purulent discharge, and preauricular adenopathy.

Lohr et al\(^3\) compared trimethoprim-polymyxin B, gentamicin, and sulfacetamide (all as ophthalmic solutions) in 158 children and young adults aged 2 months to 22 years. The three agents showed comparable clinical cure rates, using measures similar to those in the Gigliotti et al\(^2\) study, at both 3 to 6 days and 2 to 7 days posttherapy. Trimethoprim-polymyxin B was associated with a significantly higher organism eradication rate for *H influenzae* compared with either gentamicin or sulfacetamide.

Other studies support these findings, although they were performed in groups of patients that included older adults as well. Gibson\(^10\) compared trimethoprim-polymyxin B, neomycin-polymyxin-gramicidin, and chloramphenicol ophthalmic solutions in 230 patients aged 1 to 70 years. They found that trimethoprim-polymyxin B was as effective as neomycin-polymyxin-gramicidin and more effective than chloramphenicol in reducing the signs and symptoms of bacterial conjunctivitis. In contrast, Van Rensburg et al\(^11\) reported that trimethoprim-polymyxin B ophthalmic solution was as effective as chloramphenicol ophthalmic solution in improving the signs and symptoms of bacterial conjunctivitis in 40 patients aged 8 to 70 years. Equivalent efficacy also was reported in studies\(^12,13\) comparing trimethoprim-polymyxin B ophthalmic ointment with chloramphenicol ophthalmic ointment.

Regarding eradication of isolated pathogens in these studies, all the ophthalmic antimicrobial agents were effective. As is also true in clinical practice, however, pathogens were not often present on Gram stain or culture media.\(^2,3,10-13\)

In conclusion, the pediatricians in our survey who prescribed trimethoprim-polymyxin B ophthalmic solution for children with presumed acute bacterial conjunctivitis reported that this medication was effective and well tolerated. Trimethoprim-polymyxin B is effective against both gram-positive and gram-negative organisms, including *S pneumoniae* and *H influenzae*, the most prevalent bacterial pathogens in pediatric patients. Our survey results support clinical research findings on the efficacy and safety of trimethoprim-polymyxin B ophthalmic solution for the treatment of acute bacterial conjunctivitis in infants and children.

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REFERENCES


3. Lohr JA, Austin BA, Grossman M, et al. Comparison of three topical antimicro-

880


