

Eye disorders: bacterial conjunctivitis

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None declared

QUESTIONS: What are the effects of empiric treatment with antibiotics in adults and children with suspected bacterial conjunctivitis? What are the effects of antibiotics in adults and children with culture-positive bacterial conjunctivitis?

INTERVENTIONS

Beneficial

Topical antibiotics (fluoroquinolones, polymyxin B sulfate combinations, aminoglycosides, and fusidic acid [fusidate sodium])

Trade-off

Topical chloramphenicol

DEFINITION

Conjunctivitis is any inflammation of the conjunctiva, generally characterized by irritation, itching, foreign body sensation, and tearing or discharge. Bacterial conjunctivitis may usually be distinguished from other types of conjunctivitis by the presence of a yellow-white mucopurulent discharge. Usually a papillary reaction—small bumps with fibrovascular cores on the palpebral conjunctiva, appearing grossly as a fine velvety surface—is also seen. Bacterial conjunctivitis is usually unilateral, as opposed to viral conjunctivitis that often starts in 1 eye and spreads to the other. This review covers only nongonococcal bacterial conjunctivitis.

INCIDENCE/PREVALENCE

We found no good evidence on the incidence or prevalence of bacterial conjunctivitis.

ETIOLOGY/RISK FACTORS

Conjunctivitis may be infectious (caused by bacteria or viruses) or allergic. In adults, bacterial conjunctivitis is less common than viral conjunctivitis, although estimates vary widely (viral conjunctivitis has been reported to account for 8% to 75% of cases of acute conjunctivitis).¹⁻³ *Staphylococcus* species are the most common bacterial pathogens,

Summary points

- Bacterial conjunctivitis is usually self-limiting.
- In people with suspected bacterial conjunctivitis, 1 systematic review found limited evidence from 1 randomized controlled trial (RCT) that topical norfloxacin use was associated with a significantly higher rate of clinical and microbiologic improvement than placebo. Comparative RCTs found no significant difference between different topical antibiotics in rates of clinical or microbiologic cure.
- In people with bacterial conjunctivitis proved on culture, RCTs found faster clinical and microbiologic improvement with topical ciprofloxacin and ofloxacin than with placebo. Ofloxacin was associated with reduced relapse rate compared with placebo. Comparative RCTs found no significant difference between topical lomefloxacin and ciprofloxacin in clinical and microbiologic cure rates. One RCT found fusidate sodium to be superior to chloramphenicol.
- Chloramphenicol is the only topical antibiotic possibly associated with serious systemic adverse effects (aplastic anemia).
- We found no trials that examined the potential growth of resistant organisms from the use of antibiotics in bacterial conjunctivitis.

followed by *Streptococcus pneumoniae* and *Haemophilus influenzae*.^{4,5} In children, bacterial conjunctivitis is more common than viral and is mainly caused by *H influenzae*, *S pneumoniae*, and *Moraxella catarrhalis*.^{6,7}

PROGNOSIS

Most bacterial conjunctivitis is self-limiting. In a systematic review of RCTs (primary sources *Cochrane Controlled Trial Register* [updated April 1999], Medline, bibliographies of identified trials, Science Citation Index, and personal contacts with investigators and pharmaceutical companies), 64% of people (99% confidence interval [CI], 54%-73%) had clinical cure or significant improvement on placebo within 2 to 5 days.⁸ Some organisms cause corneal or systemic complications, or both; otitis may develop in 25% of children with *H influenzae* conjunctivitis,⁹ and systemic meningitis may complicate primary meningococcal conjunctivitis in 18% of people.¹⁰ Conjunc-

tivitis in children is more likely to be bacterial than viral, warranting heightened awareness of possible systemic complications.

AIMS

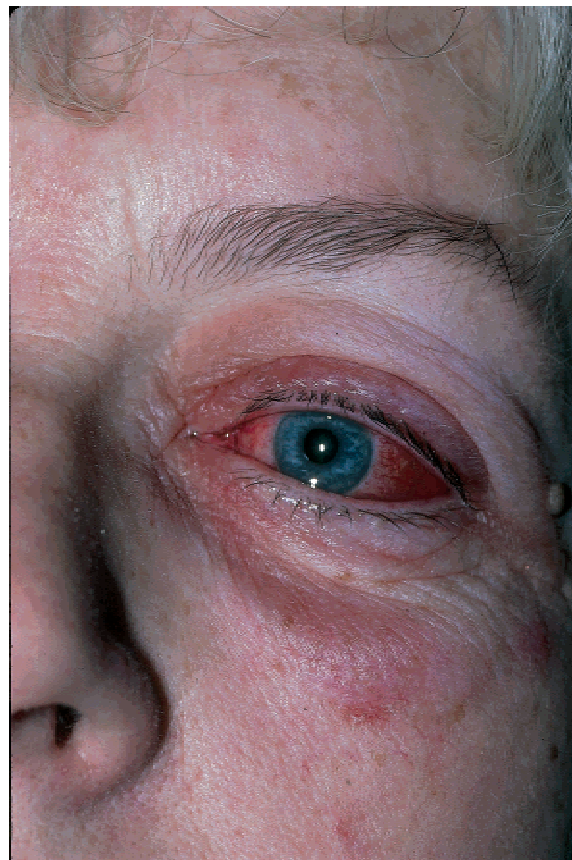
To achieve rapid resolution of inflammation and to prevent complications with minimal adverse effects of treatment.

OUTCOMES

Time to cure or improvement. **Clinical signs or symptoms:** hyperemia, discharge, papillae, follicles, chemosis, itching, pain, and photophobia. Most studies used a numbered scale to grade signs and symptoms. Some studies also included evaluation by investigators and patients regarding success of treatment. **Culture results:** usually number of colonies, sometimes with reference to a threshold level. Results were often classified into categories such as eradication, reduction, persistence, and proliferation.

METHODS

Clinical Evidence search and appraisal August 1999. All identified systemic reviews and RCTs were reviewed.



The left eye of a woman with acute conjunctivitis and periorbital edema

QUESTION: What are the effects of empiric treatment with topical antibiotics in adults and children with suspected bacterial conjunctivitis?

One systematic review found limited evidence from 1 RCT that topical norfloxacin was associated with a significantly higher rate of clinical and microbiologic improvement than placebo. Comparative RCTs found no significant difference between different topical antibiotics in rates of clinical or microbiologic cure.

Benefits

Versus placebo: We found 1 systematic review (updated in 1999) that identified 1 RCT comparing the effects of topical norfloxacin use (143 adults) versus placebo (141 adults); 50.4% of participants were culture-positive.⁸ Significantly higher rates of clinical and microbiologic cure or improvement at 5 days were obtained with norfloxacin (88.1% [95% CI, 81%-93%] vs 71.6% [95% CI, 63%-79%], $P < 0.01$). **Versus each other:** We found no systematic review. We found 18 comparative RCTs involving adults and children, and these found no significant difference between different topical antibiotics in rates of clinical or microbiologic cure (see table on the Web site www.clinicalevidence.org). Five of the RCTs (evaluating lomefloxacin, fusidic acid, rifamycin, chloramphenicol, and tobramycin sulfate) included grading by patients of effectiveness and tolerability. No significant differences were found.¹¹⁻¹⁵

Harms

The placebo-controlled RCT reported minor adverse events in 4.2% of people using norfloxacin and 7.1% using placebo (no statistical analysis available).⁵ Placebo contained a higher proportion of benzalkonium chloride (0.01% vs 0.0025% in the norfloxacin solution). One nonsystematic review described complications of topical antibiotic use.¹⁶ These included 4 reported cases of idiosyncratic aplastic anemia associated with topical chloramphenicol and 3 cases of Stevens-Johnson syndrome associated with topical sulfonamides, but no figures were given on the number of people using these drugs.

Comment

The placebo-controlled RCT did not address the effect of using topical antibiotics on antibiotic resistance, which would be of interest given the self-limiting nature of the disease.⁵ None of the trials specified their method of selecting participants. The findings may not be generalizable to primary care patients. Most trials included children and adults, and the ratio of children to adults was usually not

specified. Single-blind comparisons were used for lomefloxacin versus chloramphenicol and fusidate and norfloxacin versus fusidate. Lomefloxacin and fusidate are not available in the United States, and chloramphenicol is rarely used in the United States because of reports of idiosyncratic aplastic anemia.

QUESTION: What are the effects of topical antibiotics in adults and children with culture-positive conjunctivitis?

Randomized controlled trials in people with bacterial conjunctivitis proved on culture found faster clinical and microbiologic improvement with the use of ciprofloxacin, ofloxacin, or the combination of polymyxin B sulfate and bacitracin zinc than with placebo. The use of ofloxacin was associated with reduced relapse rates. Comparative RCTs found no significant difference between tobramycin and ciprofloxacin or between the combination of trimethoprim and polymyxin B sulfate and sulfacetamide sodium in clinical and microbiologic cure rates. One RCT found greater clinical efficacy and less microbiologic resistance with fusidate than with chloramphenicol.

Benefits

Versus placebo: We found 1 systematic review (updated 1999) that identified 3 placebo-controlled RCTs evaluating polymyxin-bacitracin, ciprofloxacin, and ofloxacin in bacterial conjunctivitis proved by culture. The review identified no trials of gentamicin sulfate that included only culture-proven conjunctivitis.⁸ One RCT of children (n = 84)¹⁷ found that in culture-proven *H influenzae* and *S pneumoniae* bacterial conjunctivitis, a higher clinical cure rate at days 3 to 5 was seen with polymyxin-bacitracin than with placebo, although by days 8 to 10, the difference was not significant (62% vs 28% at days 3-5 [$P < 0.02$], and 91% vs 72% at days 8-10 [$P > 0.05$]). The microbiologic cure rate was significantly higher with antibiotics at days 3 to 5 and 8 to 10. When antibiotics were given parenterally for concurrent problems, no significant difference was found between groups, but the numbers were too small to rule out a clinically important difference. Two other trials identified in the review did not specify the age of participants. One did not evaluate clinical outcome but found significantly greater microbiologic improvement at day 3 in people treated with ciprofloxacin (n = 177).¹⁸ One RCT published as an abstract only found significantly greater clinical and microbiologic improvement at day 2 in people treated with ofloxacin (n = 132): 64.1% versus 22.1% improved at day 2 ($P < 0.001$). It also found a lower relapse rate in people treated

with ofloxacin 2 days after treatment stopped.¹⁹ A 4th trial was published in the Japanese language and was not reviewed.²⁰

Versus each other: We found no systematic review. We found 1 RCT that did not specify the age of participants and 3 RCTs in children only. The former found no significant difference in microbiologic eradication or improvement between ciprofloxacin (n = 140) and tobramycin (n = 111); eradication or improvement occurred in 94.3% versus 91.9% ($P > 0.5$ [no CI available]).¹⁸ Clinical cure was not evaluated. Of the 3 RCTs in children, 2 found no significant difference in clinical or overall microbiologic efficacy between ciprofloxacin and tobramycin (n = 70 vs 71 [eradication, 90.1% vs 84.3%, $P = 0.29$; cure, 87% vs 89.9%, $P = 0.6$]) or between trimethoprim-polymyxin B, gentamicin, and sulfacetamide (n = 53 vs 57 vs 46 [eradication, 83% vs 68% vs 72%, $P > 0.1$; cure, 84% vs 88% vs 89%, $P > 0.1$]).^{21,22} The third (non-blinded) RCT found more clinical efficacy and less microbiologic resistance with fusidate than with chloramphenicol (n = 114 vs 25 [cure, 85% vs 48%, $P < 0.001$; resistance, 16% vs 55%, statistical analysis not provided]).²³

Harms

Of the 116 children initially enrolled in the first RCT described above, 1 was excluded because of possible allergic reaction to the ointment; the other exclusions were unrelated to adverse effects.¹⁷ In RCTs that included people with both culture-proven and suspected bacterial conjunctivitis, minor adverse events were reported with antibiotics: burning, bitter taste, pruritus, or punctate epithelial erosions (35% with tobramycin vs 20% with ciprofloxacin; no statistical detail available from abstract)²⁴; bad taste (20% with norfloxacin vs 6% with fusidate)²⁵; and stinging (50% with norfloxacin vs 37% with fusidate) and burning (gentamicin more than lomefloxacin).¹³

Comment

None of the RCTs addressed the effect on antibiotic resistance of using topical antibiotics in bacterial conjunctivitis, which would be of interest given the self-limiting nature of the disease. Furthermore, they did not report on patient-oriented outcomes or look at rates of reinfection.

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