

**EBEM Commentator**

**Nicola E. E. Schiebel, MD, FRCPC**

*From the Department of Emergency  
Medicine, Mayo Medical School, Rochester,  
MN.*

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## Use of Antibiotics in Patients With Acute Bacterial Conjunctivitis

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### SYSTEMATIC REVIEW SOURCE

This is a systematic review abstract, a regular feature of the *Annals'* Evidence-Based Emergency Medicine (EBEM) series. Each features an abstract of a systematic review from the Cochrane Database of Systematic Reviews and a commentary by an emergency physician knowledgeable in the subject area.

The source for this systematic review abstract is: Sheikh A, Hurwitz B, Cave J. Antibiotics versus placebo for acute bacterial conjunctivitis (Cochrane Review). In: *The Cochrane Library*. Issue 3. Oxford, United Kingdom: Update Software; 2002.

The *Annals'* EBEM editors assisted in the preparation of the abstract of this Cochrane systematic review as well as the Evidence-Based Medicine Teaching Points.

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### OBJECTIVE

To determine whether antibiotic therapy (topical or systemic) is superior to placebo in the treatment of patients with acute bacterial conjunctivitis.

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### DATA SOURCES

Trials were identified from the Cochrane Controlled Trials Register-Central (which contains Cochrane Eyes and Vision Group specialized register), MEDLINE, and EMBASE. The reviewers searched the reference lists of identified trial reports and contacted investigators and pharmaceutical companies to identify additional published and unpublished studies. Science Citation Index was also used to find studies that had cited the identified trials. The search is considered updated to 1999.

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### STUDY SELECTION

Studies were included if they were double-blinded, randomized, controlled trials comparing antibiotic (systemic or topical) with placebo in patients with suspected acute bacterial conjunctivitis. The diagnosis of bacterial conjunctivitis was made on clinical or microbiological grounds. "Acute" was defined as symptoms lasting less than 4 weeks duration, and participants could include patients greater than 1 month of age.

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### DATA EXTRACTION

Two authors independently selected trials for inclusion and assessed the quality of the trials. Disagreement was resolved by discussion, and

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reviewer agreement on methodologic quality assessment was documented. Data extraction was performed by one reviewer, and a second reviewer compared the extraction to the original reports. The primary outcome measures were clinical and microbiological remission rates at early (2 to 5 days) and late (6 to 10 days) follow-up. For each outcome, results were expressed as relative risk (RR) with 99% confidence intervals (CIs).

Because of a paucity of appropriate data, several planned subgroup analysis could not be completed. These included: time to symptomatic, microbiological and clinical cure, complications of conjunctivitis, adverse outcomes, compliance, and cost-effectiveness.

#### MAIN RESULTS

From 4 potentially eligible trials, 3 were included and involved 527 participants. All studies were restricted to selected specialist care patient populations. A different topical ophthalmologic antibiotic was studied in each trial. Overall, none of the studies described their randomization process, so concealed allocation could not be assessed. Also, none of the trials included an a priori sample size calculation, and no comments were made on whether those responsible for data entry and analysis were blinded to treatment allocations.

Selection of patients was based on microbiological culture confirmation in 2 studies (153 patients) and on clinical criteria in 1 study (284 patients). The clinical criteria for inclusion in this study were described as the presence of acute bacterial conjunctivitis or blephoro-conjunctivitis, with the presence of conjunctival hyperemia.

Bacterial conjunctivitis was found to be frequently self-limiting, with

clinical cure or significant improvement seen by days 2 to 5 in 64% (95% CI 57% to 71%) of those treated by placebo. Treatment with antibiotics demonstrated better rates of early clinical remission (2 to 5 days RR: 1.31; 99% CI 1.11 to 1.55). Only 1 study (66 patients) reported late clinical cure rates, and this study failed to confirm the maintenance of early benefits (6 to 10 days RR: 1.27; 99% CI 0.92 to 1.74). Microbiological cure rates were better at both early (days 2 to 5 RR: 1.71; 99% CI 1.32 to 2.21) and late (day 6 to 10 RR: 1.71; 99% CI 1.26 to 2.34) follow-up. No serious outcomes were documented in either group, providing some evidence that important sight-threatening complications such as bacterial keratitis or orbital cellulitis are infrequent in patients with acute bacterial conjunctivitis.

#### CONCLUSIONS

There is some evidence to suggest the use of broad-spectrum topical antibiotics in bacterial conjunctivitis leads to better clinical or microbiological cures. The small sample sizes and referral bias of the studies limits the strength of this conclusion for emergency clinicians. In an assessment of serious sight-threatening complications, there were none documented in either treatment group. Given the fact that bacterial conjunctivitis was also found to be frequently self-limiting, studies focusing on primary care populations and cost-effectiveness are warranted.

#### Cochrane Systematic Review Author Contact

Aziz Sheikh, MD, MSc

Department of General Practice and Primary Health

Imperial College School of Medicine at St. Mary's Norfolk Place

London, United Kingdom

E-mail [asheikh@sghms.ac.uk](mailto:asheikh@sghms.ac.uk)

#### COMMENTARY: CLINICAL IMPLICATION

The "red eye" is one of the most common ophthalmologic complaints to present to the emergency department. Once serious conditions such as iritis, keratitis, corneal ulcers, and acute angle closure glaucoma have been eliminated, conjunctivitis is often the final diagnosis. Treatment of bacterial conjunctivitis with broad-spectrum antibiotics is widely seen and is the practice recommended by standard emergency medicine textbooks.<sup>1,2</sup> Differentiation of viral from bacterial conjunctivitis requires microbiological cultures, the results of which are generally not available in a useful time period to emergency physicians. Moreover, these tests are not frequently performed in the ED because of time constraints and cost. As a result, the same emergency medicine texts recommend that all conjunctivitis be treated as if it were bacterial.

This systematic review evaluating the evidence supporting this recommendation brings up many concerns regarding its validity for emergency medicine practice. First, although there are multiple randomized, controlled trials comparing the efficacy of various topical antibiotics to each other,<sup>3</sup> there is a paucity of randomized controlled trials comparing antibiotics to placebo for bacterial conjunctivitis. The 3 studies identified in this review provide weak support for the prescription of topical antibiotics for acute conjunctivitis; however, all were carried out in specialty practices. It would be expected that primary care/emergency medicine practices would see a different spectrum of this disease; consequently, the results may not be generalized to the ED setting. Additionally, because cultures are seldom obtained in the ED, the proportion of patients with viral conjunctivitis misdiagnosed as

bacterial is unknown. Many of the patients treated with placebo improved within 2 to 5 days, and no serious complications occurred even in the placebo group. None of the studies addressed the overall incidence of antibiotic-induced adverse reactions such as corneal hyperemia, inflammation, and punctate corneal staining. This is an area of potential concern because the only data addressing this concern are more than 20 years old. At that time, adverse external ocular effects of topical ophthalmic medications were estimated to be between 13% and 16%.<sup>4</sup> Contemporary risks are largely unknown. Finally, there is increasing concern that inappropriate use of antibiotics leads to bacterial resistance and unnecessary health care costs.<sup>5</sup>

Given the evidence presented in this review, no clear conclusions can be made about the role of antibiotics for patients presenting to the ED with bacterial conjunctivitis. Further research is urgently needed to define whether the benefit seen in specialty practice exists in emergency medicine practice. Cost-benefit analysis also needs to be undertaken, given the benign course of most bacterial conjunctivitis cases. It may be that only a selected population warrants treatment, for instance, those who do not improve on their own after 5 days.

#### TAKE HOME MESSAGE

There is weak evidence to conclude that broad-spectrum topical antibiotics lead to better clinical and microbiological cure rates in bacterial conjunctivitis compared with placebo. These results are tempered by the fact that all patients studied were treated in a specialty practice environment. Moreover, bacterial conjunctivitis was frequently found to be self-limiting, and serious complications were not observed in

either treatment groups. Therefore, their overall benefit in the emergency/primary care setting is less clear.

#### EBEM Commentator Contact

Nicola E. E. Schiebel, MD, FRCPC  
 Department of Emergency Medicine  
 Mayo Clinic  
 Rochester, MN  
 E-mail [schiebel.nicola@mayo.edu](mailto:schiebel.nicola@mayo.edu)

#### EVIDENCE - BASED MEDICINE TEACHING POINTS

**Selection bias.** Selection bias can occur in both systematic reviews and individual studies. In systematic reviews, it refers to a systematic error in the selection of studies for inclusion and exclusion in a review. "Publication bias" is one form of selection bias. Most commonly, Cochrane reviews attempt to reduce selection bias by conducting a thorough search of the literature followed by independent reviewers selecting trials for relevance and inclusion.

**Specialized registries.** Specialized registries are maintained by review groups in the Cochrane Collaboration to assist reviewers in their field identify all relevant references in their review topic. They differ from the CENTRAL database because they focus on a specific topic area (in this case, eyes) and filter out those trials that are not relevant to the field. They use standardized search terms applied to multiple databases, supplemented by hand searches of the leading journals, to provide an efficient, comprehensive, and user-friendly search tool.

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