Evidence-based treatment of acute infective conjunctivitis

Breaking the cycle of antibiotic prescribing

Kari Lee Visscher MScBMC **Cindy M. L. Hutnik** MD PhD **Mary Thomas** MB BS CCFP

Conjunctivitis is the inflammation of the conjunctiva and has 4 main causes—viruses, bacteria, allergens, and irritants. Of these, the acute infective causes (viruses and bacteria) are the most frequently encountered ocular disorders in primary care, making up 1% to 2% of all family medicine consultations.[1,2] Bacterial conjunctivitis is relatively less common than viral conjunctivitis, especially in adults. Other causes of "acute red eye" (**Table 1**), such as idiopathic iritis and acute angle closure glaucoma, are often incorrectly diagnosed and managed with topical antibiotics by non-ophthalmologists.

The most prominent symptoms of acute infective conjunctivitis include mild pruritus, foreign body sensation, and mild photophobia. The most prominent signs include crusted eyelids that are often matted shut, especially after sleep, generalized conjunctival injection, and either watery or purulent discharge from one or both eyes, but no loss of visual acuity.[3] This presentation usually makes the diagnosis straightforward; however, most family physicians recognize the difficulty in clinically differentiating a viral from a bacterial infection.[4,5]

This diagnostic difficulty has been highlighted well in a Dutch cohort study involving 177 adults with suspected acute bacterial conjunctivitis. An eye swab was taken from each infected eye and cultured. The cultures showed that bacterial pathogens were present in only 32% of cases, a result that was less than the 50% (95% confidence interval 45% to 54%) pooled prevalence of bacterial pathogens found in 4 randomized trials of patients with suspected acute bacterial conjunctivitis.[4] Essentially, despite having clinically suggestive signs and symptoms of bacterial

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Abstract

OBJECTIVE To discover the best treatments for acute infective conjunctivitis and to discern whether antibiotics are necessary for the resolution of bacterial conjunctivitis in particular.

QUALITY OF EVIDENCE MEDLINE, EMBASE, and the Cochrane Database of Systematic reviews were searched. Findings were limited to full-text articles from core clinical journals in the English language, and are based on level I or level II evidence. *Clinical Evidence* was also searched, from which moderate-quality results have been cited.

MAIN MESSAGE Infective conjunctivitis should be managed conservatively, with antibiotics prescribed either after a delayed period if symptoms do not improve within 3 days of onset, or not at all. This approach helps to prevent the medicalization of the condition (reducing consultations for future occurrences) and discourages the unnecessary use of antibiotics, which might delay diagnosis of other serious red eye conditions. Physicians and patients should be educated on the self-limiting nature of the condition to increase compliance with conservative treatment and change the management expectations of parents and schools.

CONCLUSION Acute infective conjunctivitis is the most common ocular complaint dealt with in family practice; its viral and bacterial etiologies are difficult to distinguish on clinical grounds alone. Evidence suggests that properly educating patients with written information materials is the most effective way to manage this simple ailment and increase patient satisfaction.

Résumé

OBJECTIF Établir les meilleurs traitements contre la conjonctivite aiguë infectieuse et déterminer si les antibiotiques sont requis pour guérir la conjonctivite bactérienne.

QUALITÉ DES PREUVES On a consulté MEDLINE, EMBASE et la *Cochrane Database of Systematic reviews*. On a retenu seulement les articles complets de revues cliniques importantes de langue anglaise présentant des preuves de niveaux I ou II. On a également rapporté certains résultats de qualité moyenne provenant de *Clinical Evidence*.

PRINCIPAL MESSAGE La conjonctivite infectieuse devrait être traitée de façon conservatrice, les antibiotiques devant être utilisés seulement après 3 jours de traitement sans amélioration ou pas du tout. Cette approche permet de prévenir la médicalisation de cette affection (et de réduire les consultations ultérieures) et décourage l'utilisation non nécessaire d'antibiotiques, qui pourrait empêcher le diagnostic précoce d'une autre condition d'œil rouge sévère. Il importe d'éduquer médecins et parents sur la guérison spontanée habituelle de cette affection afin d'augmenter l'observance du traitement conservateur et de modifier les attentes des parents et des écoles en la matière.

CONCLUSION La conjonctivite infectieuse aiguë est l'affection oculaire la plus souvent rencontrée en médecine familiale; cliniquement, il est difficile de distinguer si la cause est virale ou bactérienne. Les preuves suggèrent que le meilleur moyen de traiter cette affection bénigne et de satisfaire les patients consiste à fournir aux patients des documents d'information appropriés.

conjunctivitis, the diagnosis can be incorrect in approximately 50% of cases. Further, bacteria that reside among the normal ocular flora can result in "false positives" when microbiologic tests are performed.

Pathogenic ambiguity, coupled with the belief that bacterial infections require prescription medication, results in treatment of most, if not all, presumed cases of infective conjunctivitis with topical ophthalmic antibiotics.[2,6] The disadvantage of this approach is the possible inappropriate treatment of viral conjunctivitis with antibiotics, which raises concerns of antibiotic resistance, cost-effectiveness, and potential increase of complications due to ocular or systemic antibiotic use.[7-9] Moreover, treatment of all red eyes with topical antibiotics can result in a delay in diagnosis of other noninfective conditions resembling conjunctivitis (**Table 1**). Conditions such as iritis and acute angle closure glaucoma can have serious long-term complications if not promptly diagnosed and managed.

If the rationale for overprescribing antibiotics is to cover any chance of bacterial causes, then one must consider whether antibiotics are even necessary for the resolution of bacterial conjunctivitis. The following paper aims to review the evidence to discover the best treatments for acute infective conjunctivitis.

Case description

A 5-year-old boy presents with a 3-day history of watery discharge from his right eye. The eye is red. Similar findings have been demonstrated in his left eye as of that morning. He is not particularly photophobic and his eyes are not itchy. He is healthy, but just got over an upper respiratory tract infection approximately 3 days ago.

Table 1. Management of red eye in primary care

ACTION	CONDITION	DESCRIPTION
Referral	Acute angle closure glaucoma	Severe ocular pain, systemic symptoms (eg, nausea, vomiting, headache), decreased vision, colour haloes around lights, fixed mid-dilated pupil, cloudy cornea, and raised intraocular pressure
	Uveitis	Sudden onset pain, photophobia, blurred vision, circumcorneal congestion, tenderness on palpation, meiotic pupil, and decreased intraocular pressure with flare
	Scleritis	Severe pain, ocular tenderness, and bluish-red scleral discolouration; associated with autoimmune illnesses (eg, rheumatoid arthritis)
	Keratitis	Ocular pain, redness, decreased vision, and white lesions (ulcers); fluorescein staining is typically indicated. Often secondary to trauma or wearing contact lenses
	Other	Chemical burns, penetrating trauma, endophthalmitis, orbital cellulitis, hyphema, or conjunctivitis that does not resolve within 7-10 days of symptom development
Treatment	Herpes simplex conjunctivitis	Painful vesicular rash over V1 distribution of trigeminal cranial nerve that requires treatment with antivirals and referral to an ophthalmologist, especially if Hutchinson sign is present
	Hyperacute gonococcal conjunctivitis	Hyperacute red eye with severe purulent discharge; requires conjunctival scrapings for culture and sensitivity, then medical management of patient and contacts. Follow up daily and consider referral if there is no improvement
	Chlamydial (inclusion) conjunctivitis	Affects sexually active teens and young adults as well as neonates (typically from developing countries). Mucopurulent keratoconjunctivitis unresponsive to antibiotics. Requires treatment of local infection and assessment for systemic infection
Reassurance	Conjunctivitis	Mild discomfort, no visual changes. Bacterial—purulent discharge; viral—preauricular node; allergic—pruritus and particularly watery discharge (usually both eyes). For infectious cases, encourage good hand and eye hygiene. If suspected bacterial cause does not improve 3 days after symptoms begin, consider ophthalmic antibiotics. If symptoms do not improve in 7-10 days, refer
	Dry eye	Foreign body sensation worsened with dry air and improved with artificial tear eyedrops
	Episcleritis	Mild irritation and photophobia, hyperemia or diffuse redness in episcleral vessel, and self-limiting, with or without NSAIDs
	Blepharitis	Inflammation of eyelid margin causing red, itchy, crusted lids, with or without abnormal eyelash growth, colour, or loss. Encourage eyelid hygiene
	Subconjunctival hemorrhage	Spontaneous or traumatic. No specific treatment, but possible contributory factors
	Gland infection	Boil-like lesions on lid or more chronic rubbery, nontender chalazions (hordeolum or stye) Hot compresses might help lesions rupture and drain

NSAID—nonsteroidal anti-inflammatory drug, V1—fifth cranial nerve, ophthalmic division.

On examination, the patient is not in acute distress. He is afebrile, has normal visual acuity, and demonstrates moderate bilateral conjunctival injection and tender preauricular nodes.

The patient's father wants a prescription for ophthalmic antibiotics because they have worked before; the boy needs 24 hours of treatment before he can return to school.

Sources of information

MEDLINE (from January 1950), EMBASE (from January 1980), and the Cochrane Database of Systematic Reviews (from January 1950) were searched until May 2009 using the following MeSH terms: *conjunctivitis* with *bacterial, diagnosis, epidemiology,* and *drug therapy; conjunctivitis* with *viral, diagnosis, epidemiology,* and *drug therapy; family practice* with *standards, statistics,* and *numerical data;* and *physician practice patterns.* Also, for information on patient education materials, the MeSH terms searched were *patient education* with *methods, pamphlets, family practice, organization and administration,* and *primary health care.* The results of the searches were limited to full-text articles from core clinical journals in the English language. The term *conjunctivitis, bacterial* was searched in *Clinical Evidence* using the full review list option; the results used in this paper are based on a January 2007 search. Finally, the Guidelines Advisory Committee was searched using the terms *conjunctivitis, red eye,* and *pink eye,* but no results were found. All research cited in this paper is based on level I or II evidence, and the information cited from *Clinical Evidence* is based on moderate-quality evidence.

Main message

According to the evidence, antibiotics are not particularly necessary for the resolution of bacterial conjunctivitis, at least not for most patients presenting in primary care. A *Clinical Evidence* summary of a Cochrane review of 3 randomized controlled trials (RCTs) and 1 subsequent RCT suggests there is moderate-quality evidence that topical antibiotics are no more effective than placebo at increasing clinical cure rates in people with suspected bacterial conjunctivitis at days 5 to 7.[6] Further, level I evidence shows high spontaneous remission rates, marginal benefits, and low risk of adverse outcomes in patients not treated with antibiotics.[2,4,6,7,10] Although there is empirical evidence to suggest topical antibiotics might have marginal benefits as well,[6] the recommended management strategy is to delay antibiotic use and promote supportive care, such as frequent eye cleansing with sterile water and cotton balls, warm water compresses, proper hand and eyelid hygiene, and temporary use of artificial tears for comfort. If the symptoms of conjunctivitis do not begin to improve within 2 days of proper supportive management, the recommendation is to then begin a topical antibiotic.[6]

This "delay" style of management was evaluated in an RCT by Everitt et al that involved 307 adults and children with acute bacterial conjunctivitis diagnosed clinically by general practitioners in southern England.[7] The study compared outcomes among patients prescribed antibiotic drops immediately, not at all, or in a delayed fashion. The delayed approach was to give a prescription that could be filled 2 to 3 days after diagnosis at the patient's discretion for worsening or persistent symptoms. The findings indicated that this approach reduced antibiotic use compared with immediate prescribing, despite similar duration and severity of symptoms. Also, the approach helped to prevent the medicalization of conjunctivitis, thereby reducing medical consultations for future episodes. The success of the delayed approach is consistent with results found in the treatment of upper and lower respiratory tract infections.[11-13] The disadvantage, however, is the added time necessary to effectively educate patients on the self-limiting nature of the condition.

Unnecessary antibiotic prescription. This might be old news for many family physicians, given that the guidelines and evidence for conservative management of conjunctivitis with judicial antibiotic use have been available for almost a decade. However, the problem is compliance.

In a retrospective study involving 195 family medicine practitioners and more than 390 000 patients in the Netherlands, 5213 new and recurrent episodes of infectious conjunctivitis were reported and 80% were prescribed ophthalmic antibiotics over a 12-month period.[1] This occurred even though the Dutch College of General Practitioners had been widely distributing

Levels of evidence

Level I: At least one properly conducted randomized controlled trial, systematic review, or meta-analysis
Level II: Other comparison trials, non-randomized, cohort, case-control, or epidemiologic studies, and preferably more than one study
Level III: Expert opinion or consensus statements

High-quality evidence: Further research is very unlikely to change confidence in the estimate of effect
Moderate-quality evidence: Further research is likely to affect confidence in the estimate of effect and might change that estimate
Low-quality evidence: Further research is very likely to affect confidence in the estimate of effect and is likely to change that estimate

accessible and clear guidelines for conservative management of red eye for the past 5 years.[14] Apparently, successful implementation of guidelines requires more than their distribution alone. The first critical step is to identify the barriers that impede positive changes in practice management. Effective communication appropriately aimed at the target audience is also essential.

In a qualitative study that conducted semistructured telephone interviews of 39 general physicians, 326 parents of children with acute infective conjunctivitis, and 223 nurseries and primary schools in Oxfordshire, UK, a network of factors that contribute to the prescribing of antibiotics was discovered.[9] Primarily, parents' beliefs about the benefits of antibiotic treatment, fueled by the desire to return their children to school, drive them to seek early treatment. They believe antibiotics are mandatory to stop infection transmission and that urgent care will prevent blindness and other serious consequences. Second, physicians' often see conjunctivitis consultations as quick and easy and use diagnostic ambiguity to justify prescribing antibiotics, which then reinforces parents' actions and beliefs.[1,9]

In the qualitative portion of Everitt et al's RCT,[7] patients identified their lack of awareness of the self-limiting nature of conjunctivitis as an important reason for requesting antibiotics. However, when properly educated about the natural progression of the condition, they were prepared to do without prescriptions for antibiotics.[7] This study highlights the importance of patient education in changing the management expectations of parents and schools, which is a finding supported by similar qualitative research.[1,9]

Policy. Another pressure for a "quick fix" is policy. For example, the updated guidelines for day nurseries from the City of Toronto's website state the following regarding pink eye:

- infectious period ranges for duration of illness or until 24 hours after treatment has started;
- signs and symptoms include redness, itching, pain, and discharge from the eye; and
- children should be excluded from the day care centre if discharge is yellow and thick (ie, pus) and until discharge is no longer present, or until appropriate medication is taken for at least 24 hours.[15]

These guidelines are problematic for 2 reasons. First, they do not reflect recent evidence-based suggestions nor do they consider allergic or irritative causes of conjunctivitis. Second, the wording of the text implies that only bacterial conjunctivitis requires exclusion from school. However, both viral and bacterial forms are contagious and should be handled with the same precautions to prevent transmission. It is generally recommended that children stay home from school until there is little to no discharge from the infected eye or eyes. The uncertainty of the pathogenesis makes the recommendation of returning to school 24 hours after antibiotic treatment rather ineffective at preventing transmission, and might contribute to the cycle of antibiotic overuse and persistent medicalization of conjunctivitis.

Patient education. Although policy improvement is necessary in certain circumstances, the proper management of conjunctivitis begins with education of the physician and the patient. Informed family physicians should know when to appropriately prescribe antibiotics and how to best educate patients. Even though the approach to patient education is best left to the individual preferences of the physician, one evidence-based suggestion is the use of information pamphlets. Written information has long been shown to have several benefits. These include an increase in patient knowledge and satisfaction, compliance with medication use and physician instruction, and a reduction in unnecessary medical visits.[16]

The benefit of information pamphlets was demonstrated in the qualitative portion of the RCT by Everitt et al.[7] The patients who received an information leaflet documented more satisfaction with the amount of information they were given and the quality of their consultation.[7] Similarly, although not specifically related to the management of conjunctivitis, an RCT of 1014 patients presenting with lower respiratory tract infections found that providing a simple leaflet regarding the natural history of the condition was an effective strategy for reducing reconsultations.[17] Furthermore, in a subsequent RCT, the use of an information leaflet supported by verbal advice proved to be a safe strategy for reducing antibiotic use in patients with acute bronchitis.[18]

Case resolution

A focused history and physical examination should be done to make a clinical diagnosis of acute infective conjunctivitis and to rule out any red flags that might indicate a different and potentially more serious condition (**Table 1**).

The parent or patient should be given a well-designed pamphlet that uses simple language and pictures to outline a description of the condition, how it is treated, reasons to make a follow-up appointment, and when to fill the postdated antibiotic prescription (if applicable).

The physician should quickly go over the most important aspects of the pamphlet with the parent or patient and answer any questions. If the delayed prescribing method is chosen, then a postdated prescription for antibiotics can be provided that the patient can use should the symptoms worsen over the next 3 days.

Conclusion

Acute infective conjunctivitis is the most common ocular complaint dealt with in family practice. This condition has both viral and bacterial causes, which can be difficult to differentiate on clinical grounds. Regardless of the cause, however, evidence suggests that the most reasonable approach to treatment in primary care is patient education and supportive management, with delayed or no prescribing of antibiotics. The patient education component, although often time-consuming, is important for changing the management expectations of parents, schools, and day cares, thereby decreasing the pressure on general practitioners to prescribe antibiotics. To help, evidence suggests that properly designed information pamphlets are a cost-effective and safe way to facilitate education and increase patient satisfaction. Further, the empowering effects of education will give parents enough confidence to manage this simple ailment at home, thereby improving the community's efforts to prevent antibiotic resistance.

Ms Visscher is a fourth-year medical student at the University of Toronto in Ontario. **Dr Hutnik** is an Associate Professor in the Department of Ophthalmology at the University of Western Ontario in London and a staff physician at St Joseph's Health Care in London. **Dr Thomas** is a Lecturer in the Department of Family and Community Medicine at the University of Toronto and a staff physician for the Southeast Toronto Family Health Team.

Contributors

Ms Visscher and **Drs Hutnik** and **Thomas** contributed to the literature review, selection and review of the studies, and preparation of the manuscript for publication.

Competing interests

None declared

Correspondence

Ms Kari Lee Visscher, Office of Health Professions Student Affairs, Faculty of Medicine, University of Toronto, 1 King's College Circle, Medical Sciences Building, Room 2171B, Toronto, ON M5S 1A8; telephone 647 271-5274; e-mail **kari.visscher@utoronto.ca**

EDITOR'S KEY POINTS

- There is a high spontaneous remission rate for bacterial conjunctivitis with proper hand and eye hygiene.
- For suspected bacterial cases, ophthalmic antibiotics should be prescribed judiciously and only if there is no improvement after 2 to 3 days of conservative management.
- Education regarding the self-limiting nature of the condition and the minimal need for antibiotics is important for changing the management expectations of parents, schools, and day cares.
- Written materials, such as pamphlets, are a safe and cost-effective way of facilitating such education, with high rates of patient satisfaction and compliance.

POINTS DE REPÈRE DU RÉDACTEUR

- La conjonctivite bactérienne à un fort taux de guérison spontanée avec une hygiène adéquate des mains et des yeux.
- Si on soupçonne une cause bactérienne, les antibiotiques ophtalmiques devraient être prescrits judicieusement, et seulement après 2 ou 3 jours de traitement conservateur.
- Il importe de renseigner parents, écoles et garderies sur la guérison spontanée habituelle de cette affection et sur le peu de nécessité des antibiotiques.
- Des dépliants ou autres documents constituent une façon sûre et efficace de diffuser ces renseignements avec un taux élevé de satisfaction et d'observance des patients.

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