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Acute infective conjunctivitis: evidence review and management advice for New Zealand practitioners

Genevieve F Oliver, Graham A Wilson, Richard J Everts

Abstract

In this review we present and discuss recent data and provide recommendations for New Zealand practitioners regarding the diagnosis and management of acute infective conjunctivitis. In particular, we discuss clinical predictors of bacterial versus viral conjunctivitis, a potential role for routine conjunctival culture, the benefits of topical antibiotic therapy for bacterial infections, delayed treatment algorithms, choice of topical antibiotic and the restriction of selected patients from work, school or early childhood care.

Most eye disease is managed solely by general practitioners (GPs), accounting for about 1.5% of their workload in the United Kingdom (UK).[1] Although only a small proportion of eye disease seen in general practice is potentially sight-threatening, one study of GPs revealed that 68% of 8279 respondents had 'some uncertainties about eyes' and 10% admitted that 'eyes scare me stiff'.[2]

Conjunctivitis is the most frequent cause of a red eye.[2] One in eight schoolchildren has an episode of acute infective conjunctivitis every year,[3] and on average GPs see a case every week.[1, 2] Despite their familiarity with this condition, there is a wide variety of approaches by GPs to the management of acute infective conjunctivitis.

We searched for relevant English-language literature using MEDLINE and bibliographies and identified a number of studies on acute infective conjunctivitis published in the last decade. In this review we examine those data and provide practical management advice for clinicians who manage adults and children with acute bacterial and viral conjunctivitis in New Zealand.

Diagnosis

The hallmark symptoms and signs of acute infective conjunctivitis are grittiness, redness and discharge with minimal or no visual disturbance. The infection is usually bilateral. Allergic conjunctivitis is typically itchy and often seasonal or reactive and accompanied by other atopic features. It is important to consider more serious eye diseases if there is unilateral red eye, severe pain, photophobia, a drop in visual acuity or recent ocular surgery or trauma.

Few well-designed studies have examined clinical predictors of bacterial versus viral conjunctivitis, despite the importance of this distinction for treatment. Rietveld et al studied 184 adults aged 18 years or older with acute conjunctivitis and found bilateral gluing of the eyelids and absence of previous conjunctivitis to correlate significantly on multivariate analysis with bacterial conjunctivitis.[4] Patel et al studied 111 children aged 1 month to 18 years with conjunctivitis and found gluey or sticky eyelids or eyelashes in the morning and purulent or mucoid discharge to independently predict

bacterial conjunctivitis.[5] The most common bacterial causes in adults and children are *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*.[3,6,7]

Swabbing the conjunctivae

No study has prospectively evaluated the utility of conjunctival culture as part of a logical algorithm in the routine management of infective conjunctivitis. Unpublished New Zealand data reveals a high correlation between preliminary (24-hour) culture results and final culture results of conjunctival swabs (> 90% positive and negative predictive value).[8] Culture results available the day after clinical evaluation could therefore be combined with clinical features to guide treatment decisions.

Certain clinical situations warrant conjunctival culture. These include infections not responding to treatment, neonatal conjunctivitis (test for *Neisseria gonorrhoea* and *Chlamydia trachomatis*), infections in contact-lens wearers, (consider *Pseudomonas aeruginosa*, *Acanthamoeba* spp. and opportunistic fungi), conjunctivitis in the setting of an outbreak (discuss testing with Public Health or Infection Control advisors) and conjunctivitis in adults who are sexually active and have other symptoms of sexually-transmitted infection or profuse purulent discharge (test for *N. gonorrhoea* and *C. trachomatis*).

Untreated, infants with ophthalmia neonatorum may develop severe ocular sequelae.[9] Serology, culture, and DNA amplification tests for adenovirus are available in New Zealand but their use is restricted to outbreak or exceptional individual situations.

Benefits of treatment

Before June 2005, more than 2 million prescriptions for ocular antibiotics were issued every year in primary care in England.[3] Given that approximately half of all conjunctivitis infections are viral and that the vast majority of bacterial conjunctivitis infections resolve spontaneously without sequelae, were these prescriptions indicated?

A meta-analysis of antibiotics versus placebo for acute bacterial conjunctivitis was published in a Cochrane review in 2006.[10] Five randomised trials including a total of 1034 participants were analysed. Clinical recovery with antibiotics was faster, especially in the first 2 to 5 days after presentation (relative risk of clinical cure 1.24; 6 patients needed treatment in order to achieve one more clinical cure than with placebo).

Six to ten days after presentation the benefit of antibiotics was less (relative risk of clinical cure 1.11; number needed to treat = 13). The benefit of topical antibiotics versus placebo was greater on microbiological cure than on clinical cure. At 2 to 5 days after presentation the relative risk of microbiological cure was 1.77; at 6 to 10 days the relative risk was 1.56.

The trial of highest methodological quality included in the Cochrane Review was a randomised, double-blind trial involving 326 children (age 6 months to 12 years) in the UK general practice setting.[3] Children were treated with chloramphenicol drops or placebo. About half a day was gained in time to resolution in those treated with antibiotic.

An additional randomised, controlled trial in 2006 (published after the Cochrane Review) assessed different management strategies for acute infective conjunctivitis.[11] Thirty general practices in southern England recruited a total of 307 adults and children over a 4-year period. Patients were randomised into three treatment groups: immediate chloramphenicol drops (every 2 hours for 2 days, then 4 times daily), delayed antibiotics (prescription to be collected at patient's discretion after 3 days) or no antibiotics. Each group was also randomised to receive an information leaflet or not as well as an eye swab or not.

Antibiotics were actually used by 99% of the immediate-antibiotic group, 53% of the delayed-antibiotic group and 30% of controls. Severity of symptoms 1 to 3 days after presentation was similar among the three treatment groups. However, duration of moderate symptoms was shorter in the immediate and delayed-antibiotic groups compared with controls (3.3 and 3.9 vs. 4.8 days, respectively). By day 8 there was no significant difference between the groups. Satisfaction with the amount of information on eye infections was greater in those who received an information leaflet and more patients also felt that the doctor dealt with their concerns well. Obtaining an eye swab increased patients' concerns about conjunctivitis.

These trials show that antibiotic treatment reduces duration of clinical illness by ½ to 1½ days. One would expect that patients would appreciate a day or so less discomfort, especially if the conjunctivitis is visually unattractive or leads to restrictions at work, school or early childhood care. Moreover, the substantial benefit of antibiotics on microbiological cure may lead to reduced transmission of pathogenic bacteria. In 2003, however, a qualitative study of patients' perceptions of acute conjunctivitis was performed in the UK,[12] which revealed that most patients who presented for treatment did so because they were unaware of its self-limiting nature.

When informed that conjunctivitis is self-limiting, most people chose to wait a few days to see if it improved, even if this resulted in a longer duration of symptoms. Patients welcomed a delayed prescription strategy as a way of potentially avoiding antibiotics and repeat visits to the doctor.

Choice of antibiotic

Randomised controlled trials of bacterial conjunctivitis reveal little or no significant difference between various antibiotics in terms of clinical efficacy.[13] Chloramphenicol is the treatment of choice in New Zealand, Australia and the United Kingdom for uncomplicated conjunctivitis in adults and children.[14–16] It has broad-spectrum activity but does not treat chlamydia or *Pseudomonas* infections.

Resistance to chloramphenicol is rare despite millions of courses having been used for decades: of 281 bacterial isolates from eye swabs submitted to Christchurch Medlab South over a 6-month period in 2008 only 3 (1%) were resistant to chloramphenicol.[7] Chloramphenicol has few side-effects.[3] A large international case-controlled study of patients with aplastic anaemia found no evidence of an association with recent topical chloramphenicol use.[17]

Fusidic acid is as effective as chloramphenicol[3] but is about four to seven times the cost and is only partly subsidised in New Zealand.[18] There are reports of emerging resistance to fusidic acid:[14] in New Zealand, for example, 14.4% of more than 11,000

Staphylococcus aureus isolates tested in 2006 were resistant to fusidic acid.[19] Moreover, one study showed that fusidic acid gel caused a burning feeling on instillation in 14% of patients.[19]

It is vital that topical antibiotics that may promote resistance to important oral agents are not used unnecessarily. Resistance develops rapidly and easily amongst *Pseudomonas aeruginosa* and other gram-negative rods to fluoroquinolones (ciprofloxacin, ofloxacin) so these should not be used outside of exceptional circumstances, such as proven pseudomonas infections.

Restriction from child-care, school, or work

The need for patients to be excluded from work, school or early childhood care is controversial and recommendations vary widely between countries, authors and institutions.[20-22] The New Zealand Ministry of Education has no guideline for children returning to school and the New Zealand Ministry of Health refers to local guidelines set by the Medical Officers of Health.

There are arguments for and against the need to restrict patients with conjunctivitis. Some reason that conjunctivitis is generally harmless and that the societal cost of restrictions is high, especially when you take into account the need for parents of children with conjunctivitis to either take leave themselves or make arrangements for childcare.

On the other hand, conjunctivitis can be uncomfortable and unsightly and both bacteria (e.g. *Streptococcus pneumoniae*)[20] and viruses (especially adenovirus)[21] can cause outbreaks in certain circumstances. An adenovirus type 8 outbreak in the Dunedin Hospital Eye Clinic in 2004 cost the District Health Board approximately $25,000 to manage and affected 15 patients and one staff member.[23]

There are few data available to guide recommendations on restriction of patients with conjunctivitis. Bacteria have frequently been isolated for a week or more after enrolment into conjunctivitis treatment trials; the isolation rate is less in groups randomised to topical antibiotics.[9] Viral excretion may persist for weeks after infection[24] and even asymptomatic or minimally symptomatic persons may contribute to transmission of organisms.[25]

The quantity of organisms and infectivity of the patient, however, decrease with time and correlate with symptoms. One mechanism for this is that as symptoms resolve the patient will less often touch his or her eye; transmission of most cases of conjunctivitis is by contaminated hand-to-hand contact. On the other hand, asymptomatic or minimally symptomatic persons may also contribute to transmission of organisms.[25]

We recommend clinicians individualise advice to patients with conjunctivitis regarding return to work, school or early childhood care based on the duration of illness, resolution of symptoms, use of topical antibiotics (only applies to proven bacterial infections), apparent infectivity of the strain (is it an outbreak?) and the patient's circumstances. For example, is the patient able to comply with good hand hygiene? Is the patient in contact with immunosuppressed persons?

Key management points

- Consider more serious eye disease if there is a unilateral red eye, decline in visual acuity, severe pain, photophobia or recent ocular surgery or trauma
- Gluing of the eyelids on waking and purulent or mucoid discharge are associated with bacterial conjunctivitis
- Preliminary conjunctival culture results (available the day after clinical evaluation) could be combined with clinical features to guide treatment decisions
- Take a conjunctival swab if the patient is not responding to therapy, a neonate, a contact-lens wearer or part of an outbreak. Also take conjunctival swabs in patients who are sexually active and there is diffuse purulent conjunctival discharge or symptoms of sexually-transmitted infection elsewhere
- Antibiotic treatment of bacterial conjunctivitis reduces duration of clinical illness by ½ to 1½ days and hastens microbiological cure
- Antibiotic treatment of bacterial conjunctivitis may be especially beneficial for patients with distressing symptoms, in outbreak situations or if the patient's infection prevents them from attending work, school or early childhood care. Once told that conjunctivitis is self-limiting, however, many patients choose to wait a few days to see if their symptoms improve without treatment
- Chloramphenicol is the recommended topical antibiotic for bacterial conjunctivitis in New Zealand as resistance among eye isolates is rare in New Zealand and it is cheap and well-tolerated
- Individualise advice to patients with conjunctivitis regarding isolation from work, school or early childhood care

Conclusion

Key management points are summarised above. Variable approaches to management of infectious conjunctivitis to date probably reflects the difficulty in clinically distinguishing bacterial from viral infections, modest benefits of antibiotic treatment and individual patient preferences regarding treatment of what is usually a benign short-lived illness. Published reports in the last decade have provided the first reliable data on clinical features of bacterial versus viral conjunctivitis, further defined the benefits of various antibiotic therapies for bacterial infections and examined the issues of patient choice and the use of delayed treatment algorithms for topical antibiotics.

Several topics require further investigation, for example, the cost-effectiveness of antibiotic treatment of bacterial conjunctivitis is unknown. There are no data available on the effectiveness of treatment with saline, ocular decongestants, povidone iodine or warm compresses. A prospective study of the use of preliminary culture results from conjunctival swab samples to guide use of topical antibiotics is underway in New Zealand.

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Author information: Genevieve F Oliver, Non-Vocational Registrar, Ophthalmology Department, Dunedin Hospital, Dunedin; Graham A Wilson, Consultant Ophthalmologist, Ophthalmology Department, Gisborne Hospital, Gisborne; Richard J Everts, Infectious Diseases Specialist and Medical Microbiologist, Nelson Hospital, Nelson

Correspondence: Graham A Wilson, Gisborne Hospital, 421 Ormond Road, Gisborne, New Zealand. Email Graham.Wilson@tdh.org.nz

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