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Bacterial conjunctivitis

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INTERVENTIONS

TREATMENTS FOR SUSPECTED BACTERIAL CONJUNCTIVITIS

Likely to be beneficial

Empirical treatment with topical antibiotics in people with suspected bacterial conjunctivitis if given to patient with advice to use after 1–2 days if symptoms do not resolve

Unknown effectiveness

Empirical treatment with ocular decongestants in people with suspected bacterial conjunctivitis New

Empirical treatment with oral antibiotics in people with suspected bacterial conjunctivitis

Empirical treatment with saline in people with suspected bacterial conjunctivitis New

Empirical treatment with warm compresses in people with suspected bacterial conjunctivitis New

TREATMENTS FOR PROVEN BACTERIAL CONJUNCTIVITIS

Beneficial

Antibiotics (topical) in people with proven bacterial conjunctivitis

Unknown effectiveness

Ocular decongestants in people with proven bacterial conjunctivitis New

Saline in people with proven bacterial conjunctivitis New

Warm compresses in people with proven bacterial conjunctivitis New

TREATMENTS FOR GONOCOCCAL CONJUNCTIVITIS

Likely to be beneficial

Antibiotics (parenteral alone or combined with topical) in people with suspected or proven gonococcal conjunctivitis * New

Unknown effectiveness

Antibiotics (oral) in people with suspected or proven gonococcal conjunctivitis New

Ocular decongestants in people with suspected or proven gonococcal conjunctivitis New

Saline in people with suspected or proven gonococcal conjunctivitis New

Warm compresses in people with clinically suspected or proven gonococcal conjunctivitis New

To be covered in future updates

Antibiotics in people with culture positive gonococcal bacterial conjunctivitis

Antibiotics in people with acanthamoeba keratitis

Combination treatments in people with acanthamoeba keratitis

Propamidine isethionate

Key Points

- Conjunctivitis causes irritation, itching, foreign body sensation, and watering or discharge of the eye.

  Most cases in adults are probably due to viral infection, but children are more likely to develop bacterial conjunctivitis than viral forms. The main bacterial pathogens are *Staphylococcus* species in adults, and *Haemophilus influenzae*, *Streptoccoccus pneumoniae* and *Moraxella catarrhalis* in children.

  A bacterial cause is more likely if there is glueing of the eyelids, and no itch.

  Contact lens wearers may be more likely to develop gram-negative infections. Bacterial keratitis occurs in up to 30/100,000 contact lens wearers.

  Gonococcal ophthalmia neonatorum can occur in up to 10% of infants exposed to gonorrhoeal exudate during delivery despite prophylaxis, and can be associated with bacteraemia and meningitis.

  Otitis media can occur in 25% of children with *H influenzae* conjunctivitis, and meningitis can develop in 18% of people with meningococcal conjunctivitis.

- Conjunctivitis resolves spontaneously within 2–5 days in more than half of people without treatment, but infectious complications can occur rarely.

- Topical antibiotics may speed up clinical and microbiological cure of bacterial conjunctivitis, but the benefit is small.

  In people with suspected, but not proven, bacterial conjunctivitis, empirical treatment with topical antibiotics may be beneficial. However, this benefit is marginal, so it is advisable to suggest to patients to only take antibiotics if symptoms do not resolve after 1–2 days.

  Clinical and microbiological cure rates are increased in the first week or so in people with culture-positive bacterial conjunctivitis, but there is no good evidence of a longer-term benefit from topical antibiotics.

Adverse effects of topical antibiotics are mild, but their effect on bacterial resistance is unknown.

- Parenteral antibiotics may cure gonoccocal ophthalmia neonatorum, although we do not know whether they are beneficial in children in Western countries, as we only found studies from Africa. Neonates will usually require investigation for concominant infections and complications.

We don't know whether ocular decongestants, saline, or warm compresses are beneficial in people with suspected or proven bacterial conjunctivitis or gonococcal conjunctivitis.

QUESTION What are the effects of empirical treatment in adults and children with suspected bacterial conjunctivitis?

OPTION EMPIRICAL TREATMENT WITH TOPICAL ANTIBIOTICS IN PEOPLE WITH SUSPECTED BACTERIAL CONJUNCTIVITIS

Cure rates

Topical antibiotics compared with placebo or no immediate treatment Topical antibiotics do not seem to be more effective at 5–7 days at increasing clinical cure rates in people with suspected bacterial conjunctivitis (moderate-quality evidence).

Topical antibiotics compared with each other Different topical antibiotics seem to be equally effective as each other at increasing clinical cure rates at 5–7 days in people with suspected bacterial conjunctivitis (moderate-quality evidence).

Topical compared with oral antibiotic We don't know whether topical antibiotics are more effective than oral antibiotics at increasing cure rates (low-quality evidence).

Different regimens of topical antibiotics compared with each other Topical gatifloxacin applied twice daily is as effective as topical gatifloxacin applied four times daily at increasing cure rates (moderate-quality evidence).

Adverse effects

Topical antibiotics are associated with burning, stinging, and bad taste.

For GRADE evaluation of interventions for bacterial conjunctivitis, see table.

Benefits:

Topical antibiotics versus placebo or no immediate treatment:
We found one systematic review and one subsequent RCT. The systematic review (search date 2005, 3 RCTs, 791 people with suspected bacterial conjunctivitis) compared topical antibiotics (norfloxacin, fusidic acid, and chloramphenicol) versus placebo. The review performed a meta-analysis including RCTs of both suspected and proven culture-positive bacterial conjunctivitis, but did not perform separate meta-analyses for these populations; we therefore report results of the indivdual RCTs here. Two RCTs identified by the review found no significant difference in clinical cure between topical antibiotics and placebo at 3 or 7 days. One RCT found that topical antibiotics significantly increased clinical cure at 5 days compared with placebo. Cure rates after 5 days were generally high in both treatment groups (see table 1).The subsequent RCT (307 adults and children with acute bacterial conjunctivitis diagnosed clinically by general practioners) compared three interventions: chloramphenicol drops prescribed immediately; chloramphenicol drops prescribed in a "delayed" fashion (to be used in 2–3 days after diagnosis at the patient's discretion for worsening or persistent symptoms), and no antibiotics. The RCT used a symptom score ranging from 0 for normal to 6 for severe (which included red eye, eye discomfort, daytime eye discharge, sticky eye on waking, eyelid swelling, altered vision, and how unwell the patient felt). The RCT found that both immediate and delayed antibiotics significantly reduced the duration of moderate symptoms compared with no antibiotics (see table 1). However, it found no significant difference between immediate or delayed antibiotics and no antibiotics in symptom scores after 1 to 3 days (symptom score 1.9 with immediate antibiotics *v* 2.1 with no antibiotics; P = 0.2; symptom score 2.0 with delayed antibiotic *v* 2.1 with no antibiotics; P = 0.4)

Topical antibiotics versus each other:
We found no systematic review but found 22 RCTs (4 published in the same article) conducted in adults and children (see table 1). All of the RCTs found no significant difference in rates of clinical cure between different topical antibiotics, and all but one also found no significant difference in rates of microbiological cure.

Topical versus oral antibiotics:
We found one RCT (80 children). It found no significant difference in clinical improvement or bacteriological failure rates between polymyxin B sulphate–bacitracin ointment plus oral placebo versus

topical placebo plus oral cefixime (see table 1). However, it may have been underpowered to detect a clinically important difference between treatments.

Different regimens of topical antibiotics versus each other:
We found one RCT. The RCT (104 people with acute conjunctivitis) found no significant difference in rate of clinical cure between gatifloxacin used twice daily versus four times daily (cure rate by fifth day: 45/52 [87%] with twice-daily dosage *v* 37/52 [71%] with four-times-daily dosage; P = 0.96).

Harms:

Topical antibiotics versus placebo:
The review gave no information on adverse effects. Two RCTs identified by the review found similar rates of adverse effects between topical antibiotics and placebo. One RCT identified by the review found that fusidic acid significantly increased adverse events compared with placebo. The subsequent RCT found that one person receiving immediate antibiotics had cellulitis; it gave no further information on adverse effects (see table 1). One large population-based prospective cohort study (4.2 million people) found that topical chloramphenicol was associated with aplastic anaemia, but that the incidence was extremely low (0.36 cases per million weeks of treatment with chloramphenicol). The incidence of aplastic anaemia was 0.04 per million weeks in people who did not take chloramphenicol. One non-systematic review reported three cases of Stevens–Johnson syndrome in people using topical sulphonamides. However, the review did not report the number of people using these drugs, making it difficult to exclude other possible causes of this condition. The RCT comparing three interventions (immediate antibiotics, delayed antibiotics or no antibiotics) reported one case of orbital cellulitis in a participant who received immmediate chloramphenicol drops.One non-systematic review (5 RCTs 1,978 adults and children) assessing safety found that moxifloxacin 0.5% given two to three times daily was associated with similar rates of overall adverse effects compared with vehicle ointment (4.7% with moxifloxacin *v* 2.6% with vehicle; no further data reported).The most common adverse effect in both groups was ocular discomfort.

Topical antibiotics versus each other:
RCTs found different rates of adverse effects (usually mild, such as burning, stinging, irritation, and bad taste) with the different agents (see table 1). Most RCTs did not assess the significance of the difference in adverse effects between groups. One non-systematic review (5 RCTs 1,978 adults and children) assessing safety found that moxifloxacin 0.5% given two to three times daily, ciprofloxacin given three times daily, or ofloxacin given four times daily were associated with similar rates of overall adverse effects (no further data about total overall adverse effects or significance assessment reported). The most common adverse effect in all groups was ocular discomfort.

Topical versus oral antibiotics:
The RCT did not report on adverse effects.

Different regimens of topical antibiotics versus each other:
The RCT found similar rates of adverse effects with two- and four-times-daily ciprofloxacin (10% in both groups, significance not reported).

Comment:

One RCT identified by the review relied primarily on self-report of clinical cure by the parents of the paediatric participants. This RCT showed reinfection (relapse or new infection) rates to be low (less than 5%) and distributed equally between chloramphenicol and placebo. Most trials above included children as well as adults, and the ratio of children to adults was usually not specified. The comparisons of lomefloxacin versus chloramphenicol and fusidic acid, the comparison of norfloxacin versus fusidic acid, and the comparison of tobramycin versus fusidic acid were single blind. One RCT found that a significantly greater proportion of participants rated topical tobramycin as more inconvenient than the viscous preparation of fusidic acid, because of a difference in the frequency of administration. The RCT also found that adherence among children was significantly higher with fusidic acid. We found no evidence on empirical antibiotic treatment specifically in contact lens wearers. In all of the RCTs, contact lens use was either not specified or was specified as an exclusion criterion, or the use of contact lenses was prohibited during the trial. None of the RCTs analysed data separately in contact lens wearers. Using eye culture swabs to guide therapy and patient information leaflets did not affect treatment outcomes.

Clinical guide:
Because of a relatively high spontaneous remission rate, there is only a marginal benefit from antibiotics for suspected bacterial conjunctivitis. The "delayed antibiotics" approach detailed in the RCT above seems to address the clinical uncertainties of the diagnosis and management of conjunctivitis most appropriately. There is no clear best choice for topical antibiotics — local microbiologic resistance patterns, cost, and other patient factors (allergies, compliance, etc.) are important consideration in addition to efficacy.

OPTION EMPIRICAL TREATMENT WITH ORAL ANTIBIOTICS IN PEOPLE WITH SUSPECTED BACTERIAL CONJUNCTIVITIS

We found no direct information about oral antibiotics in the treatment of people with suspected bacterial conjunctivitis.

For GRADE evaluation of interventions for bacterial conjunctivitis, see table.

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

OPTION EMPIRICAL OCULAR DECONGESTANTS IN PEOPLE WITH SUSPECTED BACTERIAL CONJUNCTIVITIS New

We found no direct information about ocular decongestants in the treatment of people with suspected bacterial conjunctivitis.

For GRADE evaluation of interventions for bacterial conjunctivitis, see table.

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

OPTION EMPIRICAL SALINE IN PEOPLE WITH SUSPECTED BACTERIAL CONJUNCTIVITIS New

We found no direct information about saline in the treatment of people with suspected bacterial conjunctivitis.

For GRADE evaluation of interventions for bacterial conjunctivitis, see table.

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

OPTION EMPIRICAL WARM COMPRESSES IN PEOPLE WITH SUSPECTED BACTERIAL CONJUNCTIVITIS New

We found no direct information about warm compresses in the treatment of people with suspected bacterial conjunctivitis.

For GRADE evaluation of interventions for bacterial conjunctivitis, see table.

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

QUESTION What are the effects of treatment in adults and children with bacteriologically-proven bacterial conjunctivitis?

OPTION ANTIBIOTICS (TOPICAL) IN PEOPLE WITH CULTURE-POSITIVE NON-GONOCOCCAL BACTERIAL CONJUNCTIVITIS

Cure rates
Compared with placebo Topical antibiotics (polymyxin B sulphate–bacitracin, ciprofloxacin, ofloxacin, levofloxacin, moxifloxacin) are more effective at increasing cure rates at 2–10 days in people with proven bacterial conjunctivitis (moderate-quality evidence).

Compared with each other Different topical antibiotics seem to be equally effective as each other at increasing cure rates at 5–7 days in people with proven bacterial conjunctivitis, although some antibiotics may be associated with higher rates of punctuate epithelial erosions, stinging, burning, and irritation than others (moderate-quality evidence).

For GRADE evaluation of interventions for bacterial conjunctivitis, see table.

Benefits:

Topical antibiotics versus placebo:
We found one systematic review (search date 2004, 3 RCTs, and two additional RCTsin people with culture-positive bacterial conjunctivitis, which compared antibiotics (polymyxin B sulphate–bacitracin, ciprofloxacin, ofloxacin, levofloxacin, and moxifloxacin) versus placebo (see table 1). The review performed a meta-analysis including RCTs of both suspected and proven culture-positive bacterial conjunctivitis, but did not perform separate meta-analyses for these populations; we therefore report results of the individual RCTs here. All but one of the RCTs in people with culture-positive bacterial conjunctivitis (579 people) found that topical antibiotics (ciprofloxacin, levofloxacin, moxifloxacin, ofloxacin) significantly increased clinical and microbiological cure rates over 2–10 days compared with placebo.One RCT (18 people) found that a significant increase in clinical cure at 3–5 days with polymyxin B sulphate plus bacitracin compared with placebo was not sustained at 8–10 days. This RCT also found that, in a separate analysis of people already receiving systemic antibiotics for culture-positive bacterial conjunctivitis, there was no significant difference in clinical or microbiological cure at 3–5 days between adding polymyxin B sulphate–bacitracin and adding placebo.

Topical antibiotics versus each other:
We found no systematic review but found eight RCTs (see table 1).Most RCTs found no significant difference between different topical antibiotics in clinical or microbiological cure rates. Two RCTs found no significant difference in cure rates between ciprofloxacin and tobramycin after 7 days; one assessed both clinical and microbiological cure rates, the other reduction or eradication of bacteria. A third RCT found that topical fusidic acid significantly increased clinical cure rate compared with chloramphenicol. The fourth and fifth RCTs comparing topical levofloxacin versus ofloxacin found inconclusive results. The fourth RCT found that topical levofloxacin for 5 days significantly increased microbiological cure rate compared with topical ofloxacin, but found no significant difference in clinical cure rate at 6–10 days, and the fifth RCT found similar clinical improvement rates, and no significant difference in time until improvement, between levofloxacin and ofloxacin. The sixth RCT found no significant difference in symptom resolution after 7 days between lomefloxacin and ofloxacin. The seventh RCT found that topical netilmicin significantly increased clinical cure rate after both 5 and 10 days compared with topical gentamicin. The eighth RCT compared three topical antibiotics: trimethoprim–polymyxin B sulphate, gentamicin, and sulfacetamide (sulphacetamide). It found no significant difference between antibiotics in clinical or microbiological cure rates after 2–7 days.

Harms:

Topical antibiotics versus placebo:
The RCTs found minimal and infrequent adverse effects, with no significant differences between topical antibiotics and placebo (see table 1).

Topical antibiotics versus each other:
The RCTs found infrequent adverse effects with the different topical antibiotics, with no significant differences between the different topical antibiotics reported (see table 1).The harms of the different topical antibiotics are unlikely to differ between people with suspected and culture-proven bacterial conjunctivitis (see also harms of topical antibiotics in people with suspected bacterial conjunctivitis).

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. The ages of the people in the studies were not always specified. In most of the RCTs, people were randomised and began treatment before their culture results were available, and people with negative baseline culture results were excluded from the efficacy analyses. Therefore, these results may not be generalisable to situations where treatment is not initiated until culture results are known, because of the delay in treatment. We found no studies that examined this option. The harms data for topical antibiotics versus each other are not specific to culture-positive patients.We found no evidence on antibiotics specifically in contact lens wearers with culture-positive bacterial conjunctivitis. Reviewing all of the RCTs, contact lens use was either not specified or specified as an exclusion criterion, or the use of contact lenses was prohibited during the trial. None of the RCTs analysed data separately in contact lens wearers.

Clinical guide :
Antibiotics for proven bacterial conjunctivitis lead to slightly higher clinical cure rates than placebo, but there remains a high spontaneous cure rate. There is no clear best choice for topical antibi-

otics — local microbiologic resistance patterns, cost, and other patient factors (such as allergies and compliance) are important considerations in addition to efficacy.

OPTION OCULAR DECONGESTANTS IN PEOPLE WITH PROVEN BACTERIAL CONJUNCTIVITIS

New

We found no direct information about ocular decongestants in the treatment of people with proven bacterial conjunctivitis.

For GRADE evaluation of interventions for bacterial conjunctivitis, see table.

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

OPTION SALINE IN PEOPLE WITH PROVEN BACTERIAL CONJUNCTIVITIS

New

We found no direct information about saline in the treatment of treatment of people with proven bacterial conjunctivitis.

For GRADE evaluation of interventions for bacterial conjunctivitis, see table.

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

OPTION WARM COMPRESSES IN PEOPLE WITH PROVEN BACTERIAL CONJUNCTIVITIS

New

We found no direct information about warm compresses in the treatment of people with proven bacterial conjunctivitis.

For GRADE evaluation of interventions for bacterial conjunctivitis, see table.

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

QUESTION What are the effects of treatment in adults and children with clinically-proven gonococcal conjunctivitis?

OPTION ANTIBIOTICS (PARENTERAL OR TOPICAL) IN PEOPLE WITH SUSPECTED OR PROVEN GONOCOCCAL CONJUNCTIVITIS

New

Cure rates

Parenteral antibiotic plus topical antibiotic compared with parenteral antibiotic alone Parenteral antibiotic plus topical antibiotic may be no more effective at increasing cure rates in neonates with gonococcal conjunctivitis (very low-quality evidence).

Note

There is consensus that single-dose parenteral antibiotics followed by topical antibiotics at the clinician's discretion are likely to be beneficial in people with suspected or proven gonococcal conjunctivitis.

For GRADE evaluation of interventions for bacterial conjunctivitis, see table.

Benefits: We found no systematic reviews but found four RCTs, three reported in one paper. All RCTs were carried out by the same research group treating gonococcal ophthalmia neonatorum in Africa. The first RCT (122 neonates with gonoccocal conjunctivitis) compared three interventions: single-dose parenteral ceftriaxone (125 mg) alone; single-dose parenteral kanamycin (75 mg) plus topical gentamicin for 7 days; and single-dose parenteral kanamycin (75 mg) plus topical tetracycline for 7 days. The RCT found no significant difference between groups in rates of persistent or recurrent

gonococcal conjunctivitis over 14 days (0/61 [0%] with ceftriaxone *v* 2/32 [6%] with kanamycin/gentamicin *v* 1/29 [3%] with kanamycin/tetracycline; reported as not significant, P value not reported). The other three RCTs (117 neonates with gonococcal conjunctivitis) were all reported in one paper. The first RCT (53 neonates) compared parenteral kanamycin 75 mg plus topical gentamicin for 3 days versus parenteral kanamycin 75 mg plus saline washes for 3 days. It found that single-dose (75 mg) parenteral kanamycin plus topical gentamicin significantly improved bacteriological cure rate at 30 days compared with single-dose (75 mg) parenteral kanamycin alone (cure rate 87% with kanamycin/gentamicin *v* 60% with kanamycin/saline washes; P = 0.03). The second RCT (38 infants) compared single-dose parenteral kanamycin 150 mg plus topical gentamicin for 3 days versus parenteral kanamycin 150 mg plus saline washes for 3 days. It found no significant difference in bacteriological cure rate between single-dose (150 mg) parenteral kanamycin plus topical gentamicin for 3 days versus single-dose (150mg) parenteral kanamycin alone (cure rate 87% with kanamycin/gentamicin *v* 89.5% with kanamycin/saline washes; reported as not significant, P value not reported). The third RCT (26 infants) compared parenteral kandamycin 150 mg plus topical gentamycin versus parenteral kandamycin 150 mg plus topical chloramphenicol. It stated that parenteral kandamycin 150 mg plus topical chloramphenicol resulted in cure rates of 80% — similar to those reported for parenteral kandamycin 150 mg plus topical gentamycin (86%) — but did not directly assess the difference between groups.

Harms: The RCTs gave no information on adverse effects.

Comment: **Clinical guide:** In many hospital settings, antibiotic prophylaxis against gonococcal conjunctivitis — with silver nitrate or with antibacterial ointment — is part of routine care of the neonate. There is consensus that parenteral antibiotics are likely to be beneficial in people with suspected or proven gonococcal conjunctivitis. The management of gonococcal ophthalmia neonatorum is directed by guidelines based apparently in part on the trials decribed above. Ceftriaxone is recommended for parenteral treatment followed by ointment or saline washes at the clinician's discretion. There is no evidence from resource-rich countries to guide therapy beyond these guidelines. Neonates will usually require investigation for concominant infections and complications.

OPTION ANTIBIOTICS (ORAL) IN PEOPLE WITH SUSPECTED OR PROVEN GONOCOCCAL CONJUNCTIVITIS New

We found no direct information about oral antibiotics alone in the treatment of people with suspected or proven gonococcal conjunctivitis.

For GRADE evaluation of interventions for bacterial conjunctivitis, see table.

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

OPTION OCULAR DECONGESTANTS IN PEOPLE WITH SUSPECTED OR PROVEN GONOCOCCAL CONJUNCTIVITIS New

We found no direct information about ocular decongestants in the treatment of people with suspected or proven gonococcal conjunctivitis.

For GRADE evaluation of interventions for bacterial conjunctivitis, see table.

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

OPTION SALINE IN PEOPLE WITH SUSPECTED OR PROVEN GONOCOCCAL CONJUNCTIVITIS New

We found no direct information about saline in the treatment of people with suspected or proven gonococcal conjunctivitis.

For GRADE evaluation of interventions for bacterial conjunctivitis, see table.

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

OPTION WARM COMPRESSES IN PEOPLE WITH SUSPECTED OR PROVEN GONOCOCCAL CONJUNCTIVITIS New

We found no direct information about warm compresses in the treatment of people with suspected or proven gonococcal conjunctivitis.

For GRADE evaluation of interventions for bacterial conjunctivitis, see table.

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

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