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EVIDENCE TO PRACTICE

Bacterial conjunctivitis

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Clinical question: What is the best treatment for bacterial conjunctivitis?

Results: Topical antibiotics expedite recovery from bacterial conjunctivitis. The choice of antibiotic usually does not affect outcome.

Implementation: Recognition of key distinguishing features of bacterial conjunctivitis

- Pitfalls that can be recognized in the history and physical examination
- Choice of antibiotic
- When to refer for specialist treatment.

Keywords: bacterial conjunctivitis, topical antibiotics

Bacterial conjunctivitis

Definition: Bacterial conjunctivitis is inflammation of the conjunctiva as a result of bacterial infection.

Etiology: Most commonly *Staphylococcus* species in adults, and *Streptococcus pneumonia* and the Gram-negative organisms *Haemophilus influenzae* and *Moraxella catarrhalis* in children. Contact lens wearers are at particular risk for Gram-negative infections. such as *Pseudomonas aeruginosa*. *Neisseria gonorrhoeae* is primarily a neonatal etiology.

Incidence: One recent study estimates an annual incidence rate of 135 per 10,000 in the US.[1]

Economics: The same study found the estimated total direct and indirect cost of treating bacterial conjunctivitis in the US to be $589 million annually. Accounting for a 20% variation in annual incidence rate and treatment cost resulted in an estimated cost range of $377 to $857 million per year.

Level of evidence used in this summary: Systematic reviews, meta-analyses, and randomized controlled trials from 1990 to 2010.

Search sources: Ovid MEDLINE, PubMed, Cochrane Library, NHS evidence, Clinical Evidence.

Outcomes: From the patient perspective, the main outcomes are:

1. Speed of symptomatic resolution
2. Convenience of treatment
3. Avoidance of complications.

Consumer summary: Bacterial conjunctivitis is inflammation of the conjunctiva caused by direct contact with infected secretions. The most common organisms are *Staphylococcus* species, *S. pneumonia*, *H. influenzae*, and *M. catarrhalis*. It presents with conjunctival injection, mucopurulent discharge, and crusty eyelids. The diagnosis is usually clinical. The condition is often self-limiting, but there is good evidence that antibiotics improve remission rates. Most of

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the current evidence suggests that the choice of topical antibiotics and the treatment regimen do not significantly affect the rate of recovery from infection. Failure to recognize and treat bacterial conjunctivitis may lead to complications, such as keratitis or anterior uveitis.

The evidence

Do any interventions make a difference to the resolution of bacterial conjunctivitis?

Systematic reviews: 2
Meta-analyses: 1
Randomized controlled trials: 10

The Cochrane systematic review,[2] which includes a meta-analysis, concluded that "acute bacterial conjunctivitis is frequently a self-limiting condition, but the use of antibiotics is associated with significantly improved rates of clinical and microbiological remission". The systematic review by *Clinical Evidence*[3] concludes that topical antibiotics are "beneficial" in people with culture-positive nongonococcal bacterial conjunctivitis and "likely to be beneficial" when used empirically in people with suspected bacterial conjunctivitis within 1–2 days if symptoms do not resolve on their own. Oral antibiotics, ocular decongestants, warm compresses, and saline were found to be of "unknown effectiveness".

Most randomized controlled trials (see Table 1) showed that topical antibiotics accelerate bacterial eradication and help resolve the signs and symptoms of bacterial conjunctivitis. However, in two trials,[4,5] clinical recovery at seven days after presentation was found to be unaffected by the use of antibiotics, even though one of the two trials[4] still found an improvement in microbial cure rate with antibiotics.

Which antibiotics are best for accelerating resolution of bacterial conjunctivitis?

Systematic reviews: 1
Meta-analyses: 0
Randomized controlled trials: 26

Table 2 lists the antibiotics studied, along with their microbial coverage, mechanism of action, and availability. The systematic review[3] concluded that "there is no clear best choice for topical antibiotics – local microbiological resistance patterns, cost, dosing regimens, and other patient factors (such as allergies and compliance) are important considerations in addition to efficacy". Results from randomized controlled trials (Table 3) are varied, but many found similar

Table 1 Randomized controlled trials comparing antibiotics with placebo

Author	Number of patients randomized	Interventions	Outcome measures	Results
Abelson et al[4]	279	One group received azithromycin One group received "vehicle"	Clinical resolution and bacterial eradication	Higher rate of microbial and clinical cure with antibiotic.
Everitt et al[5]	307	Two groups received chloramphenicol One group received placebo	Symptomatic relief	Antibiotic decreased the duration of symptoms.
Hwang et al[6]	249	One group received levofloxacin One group received placebo	Clinical resolution and bacterial eradication	Higher rate of microbial and clinical cure with antibiotic.
Karpecki et al[7]	269	One group received besifloxacin One group received "vehicle"	Clinical resolution and bacterial eradication	Higher rate of microbial and clinical cure with antibiotic
Leibowitz[8]	177	One group received ciprofloxacin One group received placebo	Culture results	Higher rate of microbial cure with antibiotic.
Lichtenstein and Rinehart[9]	167	One group received levofloxacin One group received ofloxacin One group received placebo	Clinical resolution and bacterial eradication	Higher rate of microbial and clinical cure with antibiotics.
Miller et al[10]	284	One group received norfloxacin One group received placebo	Bacterial eradication and clinical resolution	Higher rate of microbial and clinical cure with antibiotic.
Rietveld et al[11]	181	One group received fusidic acid One group received placebo	Clinical resolution and bacterial eradication	No difference in clinical recovery rate but higher rate of microbial eradication with antibiotic
Rose et al[12]	326	One group received chloramphenicol One group received placebo	Clinical cure by day 7	No significant difference between antibiotic and placebo
Tepedino et al[13]	957	One group received besifloxacin One group received "vehicle"	Clinical resolution and bacterial eradication	Higher rate of microbial and clinical cure with antibiotic

Table 2 Topical antibiotics used to treat bacterial conjunctivitis

Antibiotic	Class	Coverage	Mechanism	Availability
Azithromycin	Macrolide	Broad-spectrum	Baceriostatic	Azasite® 1% (Inspire Pharmaceuticals Inc)
Besifloxacin	Fluoroquinolone	Broad-spectrum	Bactericidal	Besivance® 0.6% (Bausch and Lomb)
Chloramphenicol	Chloramphenicol	Broad-spectrum	Bacteriostatic	Topical drops not marketed in US Optrex Infected Eyes® 0.5% in UK
Ciprofloxacin	Fluoroquinolone	Broad-spectrum	Bactericidal	Ciloxan® 0.3% (Alcon Laboratories Inc) Ointment or drops
Fusidic acid	Protein synthesis inhibitor	Primarily Gram-positive	Bacteriostatic	Not available in US Fucithalmic® 1% (Leo Pharma) in Canada and UK
Gatifloxacin	Fluoroquinolone	Broad-spectrum	Bactericidal	Zymar 0.3% (Allergan Inc)
Gentamicin	Aminoglycoside	Primarily Gram-negative	Bactericidal	Generic 0.3% drops
Levofloxacin	Fluoroquinolone	Broad-spectrum	Bactericidal	Iquix® 1.5% (Vistakon Pharmaceuticals)
Lomefloxacin	Fluoroquinolone	Broad-spectrum	Bactericidal	Not available in US
Moxifloxacin	Fluoroquinolone	Broad-spectrum	Bactericidal	Vigamox® 0.5% (Alcon Laboratories Inc)
Neomycin-polymyxin B-gramicidin	Aminoglycoside, polymyxin and gramicidin	Broad-spectrum	Bactericidal	Neosporin® (King Pharmaceuticals Inc)
Netilmicin	Aminoglycoside	Primarily Gram-negative	Bactericidal	Not available in US
Norfloxacin	Fluoroquinolone	Broad-spectrum	Bactericidal	Chibroxin 0.3% (Merck and Co Inc) Not available in US
Ofloxacin	Fluoroquinolone	Broad-spectrum	Bactericidal	Generic 0.3% eye drops
Providone-iodine		Broad-spectrum	Bactericidal	Betadine 5% (Alcon Laboratories Inc)
Rifamycin	Rifamycin	Broad-spectrum	Bactericidal	Not available in US
Tobramycin	Aminoglycoside	Primarily Gram-negative	Bactericidal	Tobrex® 0.3% (Alcon Laboratories Inc) ointment or drops

Table 3 Randomized controlled trials comparing different topical antibiotics

Author	Number of randomized patients	Interventions	Outcome measures	Results
Adenis at al[14]	131	0.3% ciprofloxacin versus 0.3% norfloxacin	Clinical resolution and bacterial eradication	No difference between the two antibiotics
Adenis et al[15]	41	0.3% ciprofloxacin versus 1% rifamycin	Clinical resolution and bacterial eradication	Higher clinical cure rate with ciprofloxacin on day 7 (but below statistical significance: $P = 0.061$), no difference in microbial cure
Bloom et al[16]	464	Ciprofloxacin versus tobramycin	Clinical resolution and bacterial eradication	No difference between the two antibiotics
Bremond-Gignac et al[17]	150	1.5% azithromycin versus 0.3% tobramycin	Clinical resolution and bacterial eradication	Greater bacteriologic cure with azithromycin on day 3, no difference in clinical or bacteriologic cure on day 9
Chisari et al[18]	190	Ciprofloxacin versus norfloxacin	Clinical resolution and bacterial eradication	No difference between the two antibiotics
Cochereau et al[19]	1043	1.5% azithromycin for 3 days versus 0.3% tobramycin for 7 days	Clinical resolution and bacterial eradication	Higher rate of clinical cure with azithromycin on day 3, no difference in clinical or bacteriologic cure on day 9
Denis et al[20]	1043	1.5% azithromycin for 3 days versus 0.3% tobramycin for 7 days	Microbiological resolution	No difference between the two groups
Gallenga et al[21]	99	0.3% lomefloxacin BID versus 0.3% tobramycin QID	Clinical resolution and bacterial eradication	No difference between the two groups

(*Continued*)

Table 3 (*Continued*)

Author	Number of randomized patients	Interventions	Outcome measures	Results
Granet et al[22]	84 eyes of 56 patients	Polymyxin/trimethoprim QID versus 0.5% moxifloxacin TID	Relief of signs and symptoms	Faster clinical resolution with moxifloxacin
Gwon[23]	345	0.3% ofloxacin versus 0.3% tobramycin	Clinical resolution and bacterial eradication	Similar efficacy between the two treatments, more rapid symptom relief with ofloxacin
Isenberg et al[24]	459 total, 124 culture-positive for bacteria	1.25% povidone-iodine versus neomycin-polymyxin B-gramicidin	Clinical resolution	No difference between povidone-iodine and antibiotic
Jackson et al[25]	484	1% fusidic acid versus 0.3% tobramycin	Clinical resolution, bacterial eradication, compliance, subjective "convenience" of treatment	No difference between clinical or microbial resolution, higher compliance and convenience with fusidic acid among younger patients
Kernt et al[26]	276	Enhanced-viscosity 0.3% tobramycin BID versus 0.3% tobramycin QID	Clinical resolution	No difference between the two groups
Lichtenstein et al[11]	167	0.5% levofloxacin versus 0.3% ofloxacin (versus placebo)	Clinical resolution and bacterial eradication	Higher microbial eradication rate with levofloxacin in 2–11-year-old children; no difference between the two antibiotics in other age groups
Malminiemi et al[27]	45	0.3% lomefloxacin versus 1% fusidic acid	Clinical resolution and bacterial eradication	No difference in clinical recovery but higher rate of bacterial eradication with lomefloxacin after 3–5 days
McDonald et al[28]	1161	0.6% besifloxacin versus 0.3% moxifloxacin	Clinical resolution and bacterial eradication	No difference between the two groups; higher rate of eye irritation with moxifloxacin
Milazzo et al[29]	45	0.3% netilmicin versus 0.3% tobramycin	Clinical resolution and bacterial eradication	No difference in clinical resolution, better microbiologic outcome with netilmicin
Miller et al[30]	246	Norfloxacin versus chloramphenicol	Clinical resolution and bacterial eradication	No difference between the two groups
Normann et al[31]	456 newborns	1% fusidic acid versus 0.5% chloramphenicol	Clinical resolution and compliance	No difference in efficacy but better compliance with fusidic acid
Papa et al[32]	209	Netilmicin versus gentamicin	Clinical resolution and bacterial eradication	Greater efficacy rate with netilmicin
Power et al[33]	?	0.3% ciprofloxacin versus 0.5% chloramphenicol	Clinical resolution and bacterial eradication	No difference between the two groups
Protzko et al[34]	743	1% azithromycin in DuraSite versus 0.3% tobramycin	Safety, clinical resolution and bacterial eradication	Similar safety and efficacy between the two groups
Robert et al[35]	1043	1.5% azithromycin versus 0.3% tobramycin	Clinical resolution	No difference between the two groups
Schwab et al[36]	423	0.5% levofloxacin versus 0.3% ofloxacin	Clinical resolution and bacterial eradication	More rapid microbial resolution with levofloxacin, similar clinical resolution
Tabbara et al[37]	40	0.3% lomefloxacin versus 0.3% ofloxacin	Clinical resolution	No difference between the two groups
Zhang et al[38]	132	0.3% levofloxacin versus 0.3% ofloxacin	Clinical resolution and bacterial eradication	No difference between the two groups

Abbreviations: BID, twice daily; TID, three times daily; QID, four times daily.

Table 4 Randomized controlled trials comparing different regimens of treatment

Author	Number of randomized patients	Interventions	Outcome measures	Results
Friedlaender[39]	50	0.3% ofloxacin BID versus QID	Clinical resolution and bacterial eradication	No difference between the two groups
Szaflik et al[40]	120	0.5% levofloxacin TID × 5 days versus "standard regimen" (Q2H × 2 days, then Q4H × 3 days)	Clinical resolution and bacterial eradication	No difference between the two groups
Wald et al[41]	80	Oral cefixime + topical placebo versus topical polymyxin-bacitracin + oral placebo	Clinical resolution and bacterial eradication	No difference between the two groups
Yee et al[42]	104	0.3% gatifloxacin BID versus QID	Clinical resolution, bacterial eradication and safety	No difference between the two groups

Abbreviations: Q2H, two hourly; Q4H, four hourly; BID, twice daily; TID, three times daily; QID, four times daily.

clinical and microbiologic efficacy among the topical antibiotics used. Some studies found faster bacterial eradication and/or clinical recovery with fluoroquinolones, azithromycin, or netilimicin compared with the more traditional antibiotics, such as tobramycin or polymyxin B/trimethoprim or gentamicin. Some studies found differences in patient compliance with different antibiotics. Microbiologic resistance patterns can also vary and would affect efficacy rates.

Which treatment regimen works best for bacterial conjunctivitis?

Systematic reviews:	0
Meta-analyses:	0
Randomized controlled trials:	4

A few randomized controlled trials (Table 4) have focused on the effect of the treatment regimen, such as dosing, frequency, length of treatment, and route of administration, on efficacy rates. None have found a significant change in cure rate in association with the treatment regimen used.

Conclusions

Bacterial conjunctivitis often resolves on its own, but the current evidence suggests that topical antibiotics help accelerate recovery from this self-limiting disease. Topical antibiotics used for treatment of bacterial conjunctivitis have similar efficacy rates. The treatment regimen does not affect recovery from bacterial conjunctivitis. Patients may prefer a simpler regimen.

The practice

Potential pitfalls

- Contact lens wearers are predisposed to Gram-negative infections, carrying a higher risk of complications, such as bacterial keratitis. Pseudomonas and Acanthamoeba infections in contact lens wearers can lead to serious, sight-threatening complications if not recognized and treated appropriately. The contact lens storage case may be the nidus of the infection.
- If there is an associated keratitis or anterior uveitis, referral to a specialist may be recommended
- Beware of combination topical antibiotic agents that contain steroids. These should be used with extreme caution and monitored by a specialist.

Management

Bacterial conjunctivitis can be managed by nonspecialists.

Assessment

- Redness, foreign body sensation and purulent/mucopurulent discharge are common complaints; there may be itching, chemosis, or conjunctival papillae
- Ask about contact lens wear
- Assess for corneal involvement and intraocular involvement
- Conjunctival swabs can be done for Gram stain, culture, and sensitivity to clarify diagnosis, particularly in more severe or refractory cases
- Moderate to severe eye pain, photophobia, or change in visual acuity should raise suspicion for more serious causes.

Treatment

- Uncomplicated cases can be treated with a topical antibiotic such as tobramycin, trimethoprim/polymyxin B, a fluoroquinolone or chloramphenicol four times daily for 5–7 days to accelerate recovery
- Patients should be seen every 2–3 days until signs and symptoms are resolved

- Failure to respond to topical antibiotics may warrant referral to a specialist.

Indications for specialist referral

- Change in visual acuity
- Evidence of keratitis and/or anterior uveitis on slit-lamp examination
- Moderate-to-severe eye pain
- Failure to improve or worsening of symptoms in spite of treatment.

Further reading

Ehler JP, Shah CP, Fenton GL. *The Wills Eye Manual: Office and Emergency Room Diagnosis and Treatment of Eye Disease*. Baltimore, MD: Lippincott, Williams and Wilkins; 2008.

Epling J. Bacterial conjunctivitis (updated). *Clin Evid*. 2010:1–21. Available from http://clinicalevidence.bmj.com/ceweb/conditions/eyd/0704/0704_I2.jsp. Accessed 2010 Oct 27.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Smith AF, Waycaster C. Estimate of the direct and indirect annual cost of bacterial conjunctivitis in the United States. *BMC Ophthalmol*. 2009;9:13.
2. Sheikh A, Hurwitz B. Antibiotics versus placebo for acute bacterial conjunctivitis. *Cochrane Database Syst Rev*. 2006;2:CD001211.
3. Epling J. Bacterial conjunctivitis (updated). *Clin Evid*. 2010:1–21. Available from http://clinicalevidence.bmj.com/ceweb/conditions/eyd/0704/0704_I2.jsp. Accessed 2010 Oct 27.
4. Abelson MB, Heller W, Shapiro AM, et al. Clinical cure of bacterial conjunctivitis with azithromycin 1%: Vehicle-controlled, double-masked clinical trial. *Am J Ophthalmol*. 2008;145(6):959–965.
5. Everitt HA, Little PS, Smith PW. A randomised controlled trial of management strategies for acute infective conjunctivitis in general practice. *BMJ*. 2006;333(7563):321.
6. Hwang DG, Schanzlin DJ, Rotberg MH, Foulks G, Raizman MB. A phase III, placebo controlled clinical trial of 0.5% levofloxacin ophthalmic solution for the treatment of bacterial conjunctivitis. *Br J Ophthalmol*. 2003;87(8):1004–1009.
7. Karpecki P, Depaolis M, Hunter JA, et al. Besifloxacin ophthalmic suspension 0.6% in patients with bacterial conjunctivitis: A multicenter, prospective, randomized, double-masked, vehicle-controlled, 5-day efficacy and safety study. *Clin Ther*. 2009;31(3):514–526.
8. Leibowitz HM. Antibacterial effectiveness of ciprofloxacin 0.3% ophthalmic solution in the treatment of bacterial conjunctivitis. *Am J Ophthalmol*. 1991;112 Suppl 4:29S–33S.
9. Lichtenstein SJ, Rinehart M. Efficacy and safety of 0.5% levofloxacin ophthalmic solution for the treatment of bacterial conjunctivitis in pediatric patients. *J AAPOS*. 2003;7(5):317–324.
10. Miller IM, Wittreich J, Vogel R, Cook TJ. The safety and efficacy of topical norfloxacin compared with placebo in the treatment of acute, bacterial conjunctivitis. The Norfloxacin-Placebo Ocular Study Group. *Eur J Ophthalmol*. 1992;2(2):58–66.
11. Rietveld RP, ter Riet G, Bindels PJ, Bink D, Sloos JH, van Weert HC. The treatment of acute infectious conjunctivitis with fusidic acid: A randomised controlled trial. *Br J Gen Pract*. 2005;55(521):924–930.
12. Rose PW, Harnden A, Brueggemann AB, et al. Chloramphenicol treatment for acute infective conjunctivitis in children in primary care: A randomised double-blind placebo-controlled trial. *Lancet*. 2005;366(9479):37–43.
13. Tepedino ME, Heller WH, Usner DW, et al. Phase III efficacy and safety study of besifloxacin ophthalmic suspension 0.6% in the treatment of bacterial conjunctivitis. *Curr Med Res Opin*. 2009;25(5):1159–1169.
14. Adenis JP, Brasseur G, Demailly P, et al. Comparative evaluation of efficacy and safety of ciprofloxacin and norfloxacin ophthalmic solutions. *Eur J Ophthalmol*. 1996;6(3):287–292.
15. Adenis JP, Colin J, Verin P, Saint-Blancat P, Malet F. Ciprofloxacin ophthalmic solution versus rifamycin ophthalmic solution for the treatment of conjunctivitis and blepharitis. *Eur J Ophthalmol*. 1995;5(2):82–87.
16. Bloom PA, Leeming JP, Power W, Laidlaw DA, Collum LM, Easty DL. Topical ciprofloxacin in the treatment of blepharitis and blepharoconjunctivitis. *Eur J Ophthalmol*. 1994;4(1):6–12.
17. Bremond-Gignac D, Mariani-Kurkdjian P, Beresniak A, et al. Efficacy and safety of azithromycin 1.5% eye drops for purulent bacterial conjunctivitis in pediatric patients. *Pediatr Infect Dis J*. 2010;29(3):222–226.
18. Chisari G, Sanfilippo M, Reibaldi M. Treatment of bacterial conjuntivitis with topical ciprofloxacin and norfloxacin: A comparative study. *Infez Med*. 2003;11(1):25–30. Italian.
19. Cochereau I, Meddeb-Ouertani A, Khairallah M, et al. 3-Day treatment with azithromycin 1.5% eye drops versus 7-day treatment with tobramycin 0.3% for purulent bacterial conjunctivitis: Multicentre, randomised and controlled trial in adults and children. *Br J Ophthalmol*. 2007;91(4):465–469.
20. Denis F, Chaumeil C, Goldschmidt P, et al. Microbiological efficacy of 3-day treatment with azithromycin 1.5% eye-drops for purulent bacterial conjunctivitis. *Eur J Ophthalmol*. 2008;18(6):858–868.
21. Gallenga PE, Lobefalo L, Colangelo L, et al. Topical lomefloxacin 0.3% twice daily versus tobramycin 0.3% in acute bacterial conjunctivitis: A multicenter double-blind phase III study. *Ophthalmologica*. 1999;213(4):250–257.
22. Granet DB, Dorfman M, Stroman D, Cockrum P. A multicenter comparison of polymyxin B sulfate/trimethoprim ophthalmic solution and moxifloxacin in the speed of clinical efficacy for the treatment of bacterial conjunctivitis. *J Pediatr Ophthalmol Strabismus*. 2008;45(6):340–349.
23. Gwon A. Ofloxacin vs tobramycin for the treatment of external ocular infection. Ofloxacin Study Group II. *Arch Ophthalmol*. 1992;110(9):1234–1237.
24. Isenberg SJ, Apt L, Valenton M, et al. A controlled trial of povidone-iodine to treat infectious conjunctivitis in children. *Am J Ophthalmol*. 2002;134(5):681–688.
25. Jackson WB, Low DE, Dattani D, Whitsitt PF, Leeder RG, MacDougall R. Treatment of acute bacterial conjunctivitis: 1% fusidic acid viscous drops vs 0.3% tobramycin drops. *Can J Ophthalmol*. 2002;37(4): 228–237.
26. Kernt K, Martinez MA, Bertin D, et al; International Tobrex2x Group (Eu). A clinical comparison of two formulations of tobramycin 0.3% eyedrops in the treatment of acute bacterial conjunctivitis. *Eur J Ophthalmol*. 2005;15(5):541–549.
27. Malminiemi K, Kari O, Latvala ML, Voutilainen R, Miettinen A, Jauch A. Topical lomefloxacin twice daily compared with fucidic acid in acute bacterial conjunctivitis. *Acta Ophthalmol Scand*. 1996;74(3):280–284.
28. McDonald MB, Protzko EE, Brunner LS, et al. Efficacy and safety of besifloxacin ophthalmic suspension 0.6% compared with moxifloxacin ophthalmic solution 0.5% for treating bacterial conjunctivitis. *Ophthalmology*. 2009;116(9):1615–1623.e1.
29. Milazzo G, Papa V, Carstocea B, et al. Topical netilmicin compared with tobramycin in the treatment of external ocular infection. *Int J Clin Pharmacol Ther*. 1999;37(5):243–248.

30. Miller IM, Wittreich JM, Cook T, Vogel R. The safety and efficacy of topical norfloxacin compared with chloramphenicol for the treatment of external ocular bacterial infections. The Norfloxacin-Chloramphenicol Ophthalmic Study Group. *Eye*. 1992;6(Pt 1):111–114.
31. Normann EK, Bakken O, Peltola J, et al. Treatment of acute neonatal bacterial conjunctivitis: A comparison of fucidic acid to chloramphenicol eye drops. *Acta Ophthalmol Scand*. 2002;80(2):183–187.
32. Papa V, Aragona P, Scuderi AC, et al. Treatment of acute bacterial conjunctivitis with topical netilmicin. *Cornea*. 2002;21(1):43–47.
33. Power WJ, Collum LM, Easty DL, et al. Evaluation of efficacy and safety of ciprofloxacin ophthalmic solution versus chloramphenicol. *Eur J Ophthalmol*. 1993;3(2):77–82.
34. Protzko E, Bowman L, Abelson M, Shapiro A. Phase 3 safety comparisons for 1.0% azithromycin in polymeric mucoadhesive eye drops versus 0.3% tobramycin eye drops for bacterial conjunctivitis. *Invest Ophthalmol Vis Sci*. 2007;48(8):3425–3429.
35. Robert PY, Bourcier T, Meddeb-Ouertani A, et al. Efficacy assessment of azithromycin 1.5% eye drops versus tobramycin 0.3% on clinical signs of purulent bacterial conjunctivitis. *J Fr Opthalmol*. 2010;33(4):241–248.
36. Schwab IR, Friedlaender M, McCulley J, Lichtenstein SJ, Moran CT. A phase III clinical trial of 0.5% levofloxacin ophthalmic solution versus 0.3% ofloxacin ophthalmic solution for the treatment of bacterial conjunctivitis. *Ophthalmology*. 2003;110(3):457–465.
37. Tabbara KF, El-Sheikh HF, Islam SM, Hammouda E. Treatment of acute bacterial conjunctivitis with topical lomefloxacin 0.3% compared to topical ofloxacin 0.3%. *Eur J Ophthalmol*. 1999;9(4):269–275.
38. Zhang M, Hu Y, Chen F. Clinical investigation of 0.3% levofloxacin eyedrops on the treatment of cases with acute bacterial conjunctivitis and bacterial keratitis. *Yan Ke Xue Bao*. 2000;16(2):146–148.
39. Friedlaender MH. Twice-a-day versus four-times-a-day ofloxacin treatment of external ocular infection. *CLAO J*. 1998;24(1):48–51.
40. Szaflik J, Szaflik JP, Kaminska A. Levofloxacin Bacterial Conjunctivitis Dosage Study G. Clinical and microbiological efficacy of levofloxacin administered three times a day for the treatment of bacterial conjunctivitis. *Eur J Ophthalmol*. 2009;19(1):1–9.
41. Wald ER, Greenberg D, Hoberman A. Short term oral cefixime therapy for treatment of bacterial conjunctivitis. *Pediatr Infect Dis J*. 2001;20(11):1039–1042.
42. Yee RW, Tepedino M, Bernstein P, Jensen H, Schiffman R, Whitcup SM; Gatifloxacin BID/QID Study Group. A randomized, investigator-masked clinical trial comparing the efficacy and safety of gatifloxacin 0.3% administered BID versus QID for the treatment BID versus QID for the treatment of acute bacterial conjunctivitis of acute bacterial conjunctivitis. *Curr Med Res Opin*. 2005;21(3):425–431.