Topical antibiotics for acute bacterial conjunctivitis: Cochrane systematic review and meta-analysis update

Aziz Sheikh and Brian Hurwitz

ABSTRACT

Background

Uncertainty remains about the extent to which findings from our previously published systematic review and meta-analysis of double-blind, randomised controlled trials of topical antibiotics compared with placebo in the management of patients with acute bacterial conjunctivitis treated in secondary care outpatient settings are generalisable to the management of the condition in primary care settings. We updated our review, undertaking searches, methodological assessment, data extraction and analysis according to a pre-defined protocol. In addition to the previous three included studies, we identified two additional double-blind primary care trials, one which compares fusidic acid gel with placebo gel and one which compares chloramphenicol eye drops with placebo eye drops in children. Meta-analyses of clinical and microbiological remission data reveal that topical antibiotics are of benefit in improving early (days 2–5) clinical (relative risk [RR] = 1.24, 95% confidence interval [CI] = 1.05 to 1.45) and microbiological (RR = 1.77, 95% CI = 1.23 to 2.54) remission rates; later (days 6–10) data reveal that these early advantages in clinical (RR = 1.11, 95% CI = 1.02 to 1.21) and microbiological cure rates are reduced (RR 1.56, 95% CI = 1.17 to 2.09), but persist. Most cases of acute bacterial conjunctivitis resolve spontaneously. While topical antibiotics are associated with significantly improved rates of early (days 2–5) clinical remission, this benefit is marginal for later remission (days 6–10).

Keywords

acute bacterial conjunctivitis; antibiotics; meta-analysis; randomised controlled trial; systematic review.

INTRODUCTION

In 2001 we reported the findings of our systematic review and meta-analysis evaluating the effectiveness of topical antibiotics in the treatment of acute bacterial conjunctivitis and concluded that: 'Acute bacterial conjunctivitis is frequently a self-limiting condition but the use of antibiotics is associated with significantly improved rates of early clinical remission, and early and late microbiological remission'.[1] We also sounded a word of caution, arguing that 'since trials to date have been conducted in selected specialist care patient populations, generalisations of these results to a primary care based population should be undertaken with a degree of caution'.[1]

We have since sought to update our review annually. The publication earlier this year of the trial by Rose *et al*[2] and now by Rietveld *et al*, reported in this issue (page 924),[3] represents the first new available evidence on the efficacy of topical antibiotic treatment in the management of acute bacterial conjunctivitis, and we welcome this opportunity to incorporate results from these new trials into our systematic review and meta-analysis.

METHOD

Searches were undertaken by the Cochrane Eyes and Vision Group using the search strategy detailed previously.[1] The most recent searches of electronic databases were undertaken in November 2004.

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Both authors were involved with the selection of studies, methodological assessment, and data extraction as previously detailed. Quantitative analyses of outcomes were performed on an intention-to-treat basis using random effects modelling with results expressed as relative risks with 95% confidence intervals [CIs].

RESULTS

Our previously reported review incorporated data from three eligible trials.[1] The current round of searches identified two additional studies satisfying our inclusion criteria, bringing the total number of included studies to five.[2,3] A total of 1034 patients were recruited into these five double-blind, placebo-controlled trials.

Rose *et al* studied 326 children aged 6 months to 12 years with a clinical diagnosis of infective conjunctivitis recruited from 12 UK general practices.[2] Children were randomised to either 0.5% chloramphenicol eye drops or placebo eye drops with instructions to instil one drop into each child's affected eye 2 hourly for the first 24 hours when awake, and then four times daily until 48 hours after the infection had resolved. This study was judged methodologically of high quality (grade A); using an intention-to-treat analysis it found that at the primary end point of 7 days, parent assessed cure rates were 140/163 (85.9%) in the treatment group compared with 128/163 (78.5%) in the placebo group. The mean time to clinical cure was 5 days (standard deviation [SD] = 1.9) in those treated with antibiotics compared with 5.4 days (SD = 1.9) in those on placebo. This study also found that at day 7, antibiotic treatment resulted in improved rates of microbiological remission: 81/125 (64.8%) versus 69/125 (55.2%). A clinical audit conducted at 6 weeks on the 307 (94%) patients on whom data were available revealed that relapses or new episodes of infection were rare, involving 4% of those allocated to antibiotic treatment and 3% of those receiving placebo; similarly adverse events were rare in both groups, affecting 2% of those in each arm of the trial.

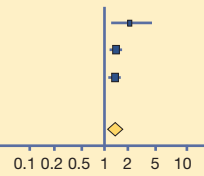
The new trial, reported in this issue of the Journal,[3] is a primary care study that recruited 181 adult patients from 25 Dutch primary care centres presenting with a red eye (whether mucopurulent discharge or glued

How this fits in

Trials of antibiotics conducted in specialist secondary care outpatient settings have shown that antibiotics are of limited value in improving clinical and microbiological outcomes in patients with acute bacterial conjunctivitis. Two new adequately powered trials conducted in primary care settings confirm that bacterial conjunctivitis is frequently self-limiting and that treatment with antibiotics offers only marginal benefits in improving clinical outcomes. The risk of adverse events in those treated with placebo eye drops appears to be low.

Table 1. Random effects meta-analysis of efficacy of topical antibiotics versus placebo in improving early (days 2–5) clinical remission.

Study or sub-category	Treatment n/N	Control n/N	RR (random) 95% CI	Weight %	RR (random) 95% CI
Gigliotti 1984	21/1984	9/32		6.18	2.20 (1.19 to 4.06)
Miller 1992	126/143	101/141		49.31	1.23 (1.09 to 1.39)
Rose 2005	123/163	107/163		44.52	1.15 (1.00 to 1.32)
Total (95% CI)	340	336		100.00	1.24 (1.05 to 1.45)

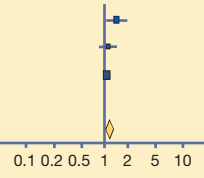


Total events: 270 (treatment), 217 (control)
Test for heterogeneity: $\chi^2 = 4.33$, degrees of freedom = 2 ($P = 0.12$), $I^2 = 53.8\%$
Test for overall effect: Z = 2.61 ($P = 0.009$)

n = number of subjects in remission. N = number of subjects tested. RR = relative risk.

Table 2. Random effects meta-analysis of efficacy of topical antibiotics versus placebo in improving late (6–10 days) clinical remission.

Study or sub-category	Treatment n/N	Control n/N	RR (random) 95% CI	Weight %	RR (random) 95% CI
Gigliotti 1984	31/34	23/32		13.26	1.27 (1.00 to 1.61)
Rietveld 2005	45/73	53/90		12.28	1.05 (0.82 to 1.21)
Rose 2005	140/163	128/163		74.46	1.09 (0.99 to 1.21)
Total (95% CI)	270	285		100.00	1.11 (1.01 to 1.21)

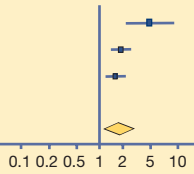


Total events: 216 (treatment), 204 (control)
Test for heterogeneity: $\chi^2 = 1.49$, degrees of freedom = 2 ($P = 0.47$), $I^2 = 0\%$
Test for overall effect: Z = 2.31 ($P = 0.02$)

n = number of subjects in remission. N = number of subjects tested. RR = relative risk.

Table 3. Random effects meta-analysis of efficacy of topical antibiotics versus placebo in improving early (days 2–5) microbiological remission.

Study or sub-category	Treatment n/N	Control n/N	RR (random) 95% CI	Weight %	RR (random) 95% CI
Gigliotti 1984	24/34	6/32		16.46	3.76 (1.77 to 8.00)
Leibowitz 2005	132/140	22/37		42.57	1.59 (1.21 to 2.08)
Miller 1992	53/76	32/67		40.97	1.46 (1.09 to 1.95)
Total (95% CI)	250	136		100.00	1.77 (1.23 to 2.54)

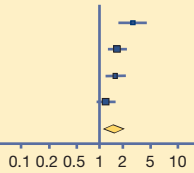


Total events: 209 (treatment), 60 (control)
Test for heterogeneity: χ^2 = 5.64, degrees of freedom = 2 (P = 0.06), I^2 = 64.5%
Test for overall effect: Z = 3.06 (P = 0.002)

n = number of subjects in remission. N = number of subjects tested. RR = relative risk.

Table 4. Random effects meta-analysis of efficacy of topical antibiotics versus placebo in improving late (6–10 days) microbiological remission.

Study or sub-category	Treatment n/N	Control n/N	RR (random) 95% CI	Weight %	RR (random) 95% CI
Gigliotti 1984	27/34	10/32		16.88	2.54 (1.48 to 4.37)
Miller 1992	59/76	35/67		30.67	1.49 (1.15 to 1.93)
Rietveld 2005	16/21	12/29		18.68	1.84 (1.12 to 3.02)
Rose 2005	81/125	69/125		33.76	1.17 (0.96 to 1.44)
Total (95% CI)	256	253		100.0	1.56 (1.17 to 2.09)



Total events: 183 (treatment), 126 (control)
Test for heterogeneity: χ^2 = 9.01, degrees of freedom = 3 (P = 0.03), I^2 = 66.7%
Test for overall effect: Z = 3.01 (P = 0.003)

n = number of subjects in remission. N = number of subjects tested. RR = relative risk.

eyelid(s)) who were randomly allocated to either one drop of fusidic acid gel 1% or placebo gel, four times daily for a week. This study is methodologically of high quality (grade A); using an intention-to-treat analysis it found that at 7 days patient assessed cure rates were 45/73 (61.6%) in the treatment group and 53/90 (58.9%) in the placebo group.

Meta-analysis of early (days 2–5) and late (days 7–10) clinical and microbiological outcomes reveals that topical antibiotics are of benefit in improving early clinical (relative risk [RR] = 0.24, 95% CI = 1.05 to 1.45) and microbiological (RR = 1.77, 95% CI = 1.23 to 2.54) remission, with these benefits being reduced, but nonetheless persisting for late clinical (RR = 1.11, 95% CI = 1.02 to 1.21) and microbiological (RR = 1.56, 95% CI = 1.17 to 2.09) remission (Tables 1–4).

DISCUSSION

These two adequately powered new trials represent a welcome addition to the evidence base for the treatment of acute bacterial conjunctivitis.[4] They confirm findings from previous outpatient-based secondary care studies that indicate that topical antibiotics are of limited efficacy in improving clinical outcomes for acute bacterial conjunctivitis. While topical antibiotics clearly have an impact on microbiological remission and (less so) on early clinical remission rates, by 6–10 days their clinical advantage is marginal. Although unanswered questions about risk of serious adverse events in those who do not receive antibiotic treatment remain to be fully addressed, on balance our earlier conclusion is strengthened by this updated systematic review and meta-analysis: acute bacterial conjunctivitis is frequently a self-limiting condition and topical antibiotic use offers only marginal benefit in improving clinical outcomes.[4,5]

Competing interests

Aziz Sheikh was a co-author on one of the new trials incorporated into this review update

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