

A randomised controlled trial of management strategies for acute infective conjunctivitis in general practice

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Abstract

Objective To assess different management strategies for acute infective conjunctivitis.

Design Open, factorial, randomised controlled trial.

Setting 30 general practices in southern England.

Participants 307 adults and children with acute infective conjunctivitis.

Intervention One of three antibiotic prescribing strategies—immediate antibiotics (chloramphenicol eye drops; $n = 104$), no antibiotics (controls; $n = 94$), or delayed antibiotics ($n = 109$); a patient information leaflet or not; and an eye swab or not.

Main outcome measures Severity of symptoms on days 1-3 after consultation, duration of symptoms, and belief in the effectiveness of antibiotics for eye infections.

Results Prescribing strategies did not affect the severity of symptoms but duration of moderate symptoms was less with antibiotics: no antibiotics (controls) 4.8 days, immediate antibiotics 3.3 days (risk ratio 0.7, 95% confidence interval 0.6 to 0.8), delayed antibiotics 3.9 days (0.8, 0.7 to 0.9). Compared with no initial offer of antibiotics, antibiotic use was higher in the immediate antibiotic group: controls 30%, immediate antibiotics 99% (odds ratio 185.4, 23.9 to 1439.2), delayed antibiotics 53% (2.9, 1.4 to 5.7), as was belief in the effectiveness of antibiotics: controls 47%, immediate antibiotics 67% (odds ratio 2.4, 1.1 to 5.0), delayed antibiotics 55% (1.4, 0.7 to 3.0), and intention to reattend for eye infections: controls 40%, immediate antibiotics 68% (3.2, 1.6 to 6.4), delayed antibiotics 41% (1.0, 0.5 to 2.0). A patient information leaflet or eye swab had no effect on the main outcomes. Reattendance within two weeks was less in the delayed compared with immediate antibiotic group: 0.3 (0.1 to 1.0) *v* 0.7 (0.3 to 1.6).

Conclusions Delayed prescribing of antibiotics is probably the most appropriate strategy for managing acute conjunctivitis in primary care. It reduces antibiotic use, shows no evidence of medicalisation, provides similar duration and severity of symptoms to immediate prescribing, and reduces reattendance for eye infections.

Trial registration Current Controlled Trials ISRCTN32956955.

Introduction

Evidence is lacking, particularly in general practice, on the effectiveness of prescribing topical antibiotics for conjunctivitis.¹ A Cochrane review showed a marginal benefit from such treatment.²

We assessed the effect of different prescribing strategies for chloramphenicol eye drops in adults and children with acute infective conjunctivitis, an information leaflet, and an eye swab. We also assessed antibiotic use, patients' beliefs in the effectiveness of antibiotics, and intention to reattend for eye infections.

Methods

Between April 2001 and April 2005 general practitioners or practice nurses in 30 general practices in Hampshire, Wiltshire, and Dorset recruited patients aged 1 year or more with acute infective conjunctivitis. (See bmj.com for exclusion criteria.)

We randomised patients to one of three treatments: immediate antibiotics (chloramphenicol eye drops every two hours for two days then four times daily), delayed antibiotics (prescription to be collected at the parents' or patients' discretion after three days), and no antibiotics (controls). The groups were also randomised to receive an information leaflet or not, creating six groups. Each patient in the six groups was randomised to an eye swab or not for microbiology.

The primary outcome measures were duration of moderately bad symptoms (days when one or more symptoms scored moderately bad or worse), mean symptom severity score on days 1-3 after consulting, and belief in the effectiveness of antibiotics for eye infections (extremely or very effective on a six point scale).

We obtained outcome data from patient completed diaries.³⁻⁵ Patients scored their symptoms (see bmj.com) for 14 days on a seven point scale. Patients also completed questions on other symptoms, antibiotic use, belief in the effectiveness of antibiotics, intention to reattend for eye infections, and personal details. We calculated a deprivation score using the participants' postcodes.

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Table 1 Main outcomes by antibiotic group for responders (adjusted for patient information leaflet and eye swab)

Outcome	No antibiotics (n=76)	Immediate antibiotics (n=85)	Difference (immediate–no antibiotics) (95% CI)	P value	Delayed antibiotics (n=89)	Difference (delayed–no antibiotics) (95% CI)	P value
Mean (SD) symptom score*	2.1 (0.9)	1.9 (0.9)	–0.2 (–0.5 to 0.1)	0.2	2.0 (1.0)	–0.1 (–0.4 to 0.2)	0.4
Mean (SD) duration of moderate symptoms (days)	4.8 (3.2)	3.3 (2.8)	0.7† (0.6 to 0.8)	0.001	3.9 (2.5)	0.8† (0.7 to 0.9)	0.002
No (%) who believe antibiotics are extremely or very effective for eye infections	23/49 (47)	47/70 (67)	2.4‡ (1.1 to 5.0)	0.03	36/65 (55)	1.4‡ (0.7 to 3.0)	0.4
No (%) who are extremely or very likely to reattend for future eye infections	26/65 (40)	49/72 (68)	3.2‡ (1.6 to 6.4)	0.001	34/84 (41)	1.0‡ (0.5 to 2.0)	1.0

*Scored on days 1–3 after consultation for acute infective conjunctivitis.

†Rate ratio.

‡Odds ratio.

Statistical analysis

We analysed data on an intention to treat basis using Stata. To determine which symptoms contributed to the symptom severity score we used factor analysis; internal reliability of the score was assessed using Cronbach’s *a*. We used multiple linear regression for the symptom severity score, multiple Poisson regression for duration of moderate symptoms, and multiple logistic regression for belief in antibiotics. We explored interactions between the intervention variables and potential confounders.

Results

Between April 2001 and April 2005, 30 general practices in Hampshire, Wiltshire, and Dorset recruited 307 adults and children with acute infective conjunctivitis to the trial. Participants were randomised to either immediate antibiotics (chloramphenicol eye drops; n=104), no antibiotics (controls; n=94), or delayed antibiotics (n=109). Two hundred and fifty patients completed diaries for outcomes (response rate 81%; see bmj.com).

The groups had similar characteristics at baseline (see bmj.com). Response rates did not differ significantly between the groups. Although responders were older than non-responders (mean (SD) 29.5 (28.4) years *v* 18.3 (18.7) years) and had lower deprivation scores (12.7 (9.8) *v* 15.9 (11.5)), including these variables in the models did not alter the estimates of effectiveness.

During the episode of conjunctivitis, antibiotics were used by 99% of the immediate group, 53% of the delayed group, and 30% of the no antibiotic group: immediate antibiotics *v* no antibiotics (odds ratio 185.4, 95% confidence interval 23.9 to 1439.2; delayed antibiotics *v* no antibiotics (2.9, 1.4 to 5.7)).

Main outcome measures

The average score for severity of symptoms on days 1–3 did not differ significantly between the groups (table 1). Duration of moderate symptoms was shorter in the immediate and delayed groups than in the controls:

controls 4.8 days, immediate antibiotics 3.3 days (risk ratio 0.7, 95% confidence interval 0.6 to 0.8), and delayed antibiotics 3.9 days (0.8, 0.7 to 0.9; table 1). See figure on bmj.com showing resolution of moderate symptoms.

The immediate antibiotic group were more likely than controls to believe that antibiotics were effective (odds ratio 2.4, 1.1 to 5.0: number needed to treat 5) and more likely to state their intention to reattend for eye infections (3.2, 1.6 to 6.4: number needed to treat 4). The delayed antibiotic group was not significantly different from the controls (table 1).

An information leaflet or eye swab did not significantly affect any outcomes (tables 2 and 3).

Patient information leaflet and eye swab

Satisfaction with the amount of information on eye infections was greater in those who received an information leaflet (odds ratio 2.4, 1.3 to 4.5). The leaflet was also associated with an increase in the patient’s perception that the doctor dealt with their concerns extremely or very well (1.9, 1.0 to 3.7) and satisfaction with the consultation (1.9, 1.0 to 3.7; see bmj.com).

Obtaining an eye swab increased patients’ concerns about conjunctivitis (1.7, 1.0 to 3.0; see bmj.com). Significant bacterial growth was detected in 69 of 138 (50%) swabs. No significant difference was found in outcome measures between those with and without bacterial growth.

Reattendance, complications, and recruitment

Overall 57 of the 307 (19%) participants reattended for conjunctivitis in the year after recruitment, 26 (9%) within two weeks. Those in the delayed antibiotic group were less likely to reattend within two weeks than those in the control group (odds ratio 0.3, 95% confidence interval 0.1 to 1.0), but no significant difference was found between the immediate antibiotic group and controls (0.7, 0.3 to 1.6).

No difference was found between high recruiters (more than 70% of cases encountered) and low recruiters in severity of presenting symptoms, sex of participants, or proportion of children participating,

Table 2 Main outcomes by patient information leaflet for responders (adjusted for antibiotic group and eye swab)

Outcome	No information leaflet (n=119)	Information leaflet (n=122)	Difference (leaflet–no leaflet) (95% CI)	P value
Mean (SD) symptom score*	1.9 (1.0)	2.0 (1.0)	0.1 (–0.2 to 0.3)	0.6
Mean (SD) duration of moderate symptoms (days)	3.9 (2.9)	4.1 (3.0)	1.0† (0.8 to 1.3)	0.9
No (%) who believe antibiotics are extremely or very effective for eye infections	51/88 (58)	55/96 (57)	1.0‡ (0.9 to 1.2)	0.8
No (%) extremely or very likely to reattend for future eye infections	57/107 (53)	52/114 (46)	0.8‡ (0.4 to 1.3)	0.3

*Scored on days 1–3 after consultation for acute infective conjunctivitis.

†Rate ratio.

‡Odds ratio.

but higher recruiters recruited older participants (mean age 31.6 *v* 24.6 years) and those with lower deprivation scores (index of multiple deprivation 11.4 *v* 14.8). Recruitment status of the patient did not affect outcome measures.

Discussion

Different prescribing strategies using chloramphenicol eye drops for acute infective conjunctivitis (immediate, none, delayed) did not affect symptom severity in the three days after consulting, but duration of moderate symptoms was less in the immediate and delayed groups. Compared with no initial offer of antibiotics (control group), antibiotic use, belief in the effectiveness of antibiotics, and intention to reattend for eye infections were higher in the immediate antibiotic group. A patient information leaflet or eye swab had no effect on the main outcome measures.

On average symptoms were scored as slight to moderate. However, antibiotics were used by 53% of the delayed antibiotic group and 30% of the controls. This was probably related to a belief in the need for antibiotics despite symptoms being mild.⁶ Whatever the reasons, no initial offer of antibiotics resulted in significant use of antibiotics.

The difference between the immediate and no antibiotic groups was one and a half days of moderate symptoms—half a day for the delayed antibiotic group. The proportion of patients cured converged, so by day 8 there was no significant difference between the groups (see bmj.com). This varies with the results of Rose et al's study,⁷ which found a 0.3 day difference in symptoms between chloramphenicol and placebo at days 2-7 after consultation. Plausible explanations are a greater placebo effect, although this is unlikely as estimates from our open trials³⁻⁵ (using identical methodology) were similar to blinded trials; Rose et al⁷ underestimated the effect of drops (our estimates are closer to the Cochrane review^{1 2}); different outcomes were measured (Rose et al did not measure duration of moderate symptoms⁷); and drops may provide lubrication and flush out pathogens (Rose et al's study used drops in both arms⁷).

Immediate prescribing seems to medicalise patients with conjunctivitis. Patients assigned to immediate antibiotics were more likely to state they would reattend for eye infections than those assigned to no or delayed antibiotics.

Delayed prescribing enables the clinical course of conjunctivitis to be discussed with patients. Our qualitative research indicated that patients' lack of awareness of the self limiting nature of conjunctivitis was an important reason for attending for antibiotics.⁶ It also

What is already known on this topic

Topical antibiotics are usually prescribed for conjunctivitis but evidence on their effectiveness is mixed

What this study adds

Delaying antibiotics for conjunctivitis in primary care was associated with reduced antibiotic use, no evidence of medicalisation, and similar severity and duration of symptoms to immediate prescribing

No initial offer of antibiotics still resulted in significant antibiotic use (30%)

Compared with no antibiotics, delayed prescribing was associated with reduced reattendance for eye infections

showed that patients were happy with delayed prescribing and about deciding whether to start antibiotics.

An information leaflet and eye swab did not affect the main outcomes. An information leaflet was, however, associated with increased satisfaction with the consultation and amount of information received and the perception that the doctor dealt with concerns well. Conversely, an eye swab increased patients' worries about their eye infection.

Strengths and limitations of the study

Our pragmatic open trial design enabled assessment of symptom resolution along with patients' responses to different strategies, belief in and use of antibiotics, and intention to reattend for eye infections. Any placebo effect was minimised by using standard advice packages.

Selective overall recruitment could limit generalisability. Not every patient with conjunctivitis was recruited. Patients from high recruiters differed in age and deprivation score from those of low recruiters, however the patient's recruitment status did not predict outcome or affect the estimates of effectiveness. Although respondents were older and had lower deprivation scores than non-respondents, neither altered the effect size.

The delayed antibiotic strategy involved participants returning to the surgery for their prescription. This may have reduced antibiotic use compared with providing the prescription immediately and advising a delay in using the drug.

Conclusion

Compared with no antibiotics delayed prescribing had the advantage of reduced antibiotic use, no evidence of

Table 3 Main outcomes by eye swab for responders (adjusted for antibiotic group and patient information leaflet)

Outcome	No eye swab (n=117)	Eye swab (n=127)	Difference (eye swab–no eye swab) (95% CI)	P value
Mean (SD) symptom score*	1.9 (0.9)	2.1 (1.0)	0.2 (–0.1 to 0.4)	0.2
Mean (SD) duration of moderate symptoms (days)	3.8 (2.9)	4.2 (3.0)	1.1† (1.0 to 1.3)	0.1
No (%) who believe antibiotics are extremely or very effective for eye infections	56/95 (59)	50/89 (56)	0.9‡ (0.5 to 1.6)	0.6
No (%) extremely or very likely to reattend for future eye infections	53/109 (49)	56/112 (50)	1.1‡ (0.6 to 1.9)	0.7

*On days 1-3 after consultation for acute infective conjunctivitis.

†Rate ratio.

‡Odds ratio.

medicalisation, similar symptom control to immediate prescribing, and reduced reattendance for eye infections.

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Prevention of postoperative nausea and vomiting by metoclopramide combined with dexamethasone: randomised double blind multicentre trial

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Abstract

Objectives To determine whether 10 mg, 25 mg, or 50 mg metoclopramide combined with 8 mg dexamethasone, given intraoperatively, is more effective in preventing postoperative nausea and vomiting than 8 mg dexamethasone alone, and to assess benefit in relation to adverse drug reactions.

Design Four-armed, parallel group, double blind, randomised controlled clinical trial.

Setting Four clinics of a university hospital and four district hospitals in Germany.

Participants 3140 patients who received balanced or regional anaesthesia during surgery.

Main outcome measures Postoperative nausea and vomiting within 24 hours of surgery (primary end point); occurrence of adverse reactions.

Results Cumulative incidences (95% confidence intervals) of postoperative nausea and vomiting were 23.1% (20.2% to 26.0%), 20.6% (17.8% to 23.4%), 17.2% (14.6% to 19.8%), and 14.5% (12.0% to 17.0%) for 0 mg, 10 mg, 25 mg, and 50 mg metoclopramide. In the secondary analysis, 25 mg and 50 mg metoclopramide were equally effective at preventing early nausea (0-12 hours), but only 50 mg reduced late nausea and vomiting (> 12 hours). The most frequent adverse drug reactions were hypotension and tachycardia, with cumulative incidences of 8.8% (6.8% to 10.8%), 11.2% (9.0% to 13.4%), 12.9% (10.5% to 15.3%), and 17.9% (15.2% to 20.6%) for 0 mg, 10 mg, 25 mg, and 50 mg metoclopramide.

Conclusion The addition of 50 mg metoclopramide to 8 mg dexamethasone (given intraoperatively) is an effective, safe, and cheap way to prevent postoperative nausea and vomiting. A reduced dose of 25 mg

metoclopramide intraoperatively, with additional postoperative prophylaxis in high risk patients, may be equally effective and cause fewer adverse drug reactions.

Trial registration Current Controlled Trials ISRCTN 31625370.

Introduction

A large clinical trial of postoperative nausea and vomiting showed that 4 mg ondansetron, 4 mg dexamethasone, or 1.25 mg droperidol were effective, and that combinations of these drugs had an additive effect.¹ Dexamethasone was recommended as the first line drug, as it is safe and cheap.

Data on metoclopramide as an antiemetic after surgery are contradictory. A meta-analysis found that an intravenous dose of 10 mg had only a marginal effect,² but because of its complex mode of action (it binds to dopamine, serotonin, and histamine receptors), metoclopramide remains an interesting drug.³ Studies have concluded that metoclopramide is ineffective in this context, but the timing of administration and use of larger doses were not investigated fully. We investigated the efficacy and safety of three doses of metoclopramide (10 mg, 25 mg, and 50 mg), on the assumption that each patient would receive basic antiemetic prophylaxis of 8 mg dexamethasone.



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