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[Intervention Review]

Delayed antibiotic prescriptions for respiratory infections

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ABSTRACT

Background

Concerns exist regarding antibiotic prescribing for respiratory tract infections (RTIs) owing to adverse reactions, cost, and antibacterial resistance. One proposed strategy to reduce antibiotic prescribing is to provide prescriptions, but to advise delay in antibiotic use with the expectation that symptoms will resolve first. This is an update of a Cochrane Review originally published in 2007, and updated in 2010 and 2013.

Objectives

To evaluate the effects on clinical outcomes, antibiotic use, antibiotic resistance, and patient satisfaction of advising a *delayed* prescription of antibiotics in respiratory tract infections.

Search methods

For this 2017 update we searched the Cochrane Central Register of Controlled Trials (CENTRAL) (the Cochrane Library, Issue 4, 2017), which includes the Cochrane Acute Respiratory Infection Group's Specialised Register; Ovid MEDLINE (2013 to 25 May 2017); Ovid Embase (2013 to 2017 Week 21); EBSCO CINAHL Plus (1984 to 25 May 2017); Web of Science (2013 to 25 May 2017); WHO International Clinical Trials Registry Platform (1 September 2017); and ClinicalTrials.gov (1 September 2017).

Selection criteria

Randomised controlled trials involving participants of all ages defined as having an RTI, where *delayed* antibiotics were compared to *immediate* antibiotics or *no* antibiotics. We defined a *delayed* antibiotic as advice to delay the filling of an antibiotic prescription by at least 48 hours. We considered all RTIs regardless of whether antibiotics were recommended or not.

Data collection and analysis

We used standard Cochrane methodological procedures. Three review authors independently extracted and collated data. We assessed the risk of bias of all included trials. We contacted trial authors to obtain missing information.

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Main results

For this 2017 update we added one new trial involving 405 participants with uncomplicated acute respiratory infection. Overall, this review included 11 studies with a total of 3555 participants. These 11 studies involved acute respiratory infections including acute otitis media (three studies), streptococcal pharyngitis (three studies), cough (two studies), sore throat (one study), common cold (one study), and a variety of RTIs (one study). Five studies involved only children, two only adults, and four included both adults and children. Six studies were conducted in a primary care setting, three in paediatric clinics, and two in emergency departments.

Studies were well reported, and appeared to be of moderate quality. Randomisation was not adequately described in two trials. Four trials blinded the outcomes assessor, and three included blinding of participants and doctors. We conducted meta-analysis for antibiotic use and patient satisfaction.

We found no differences among *delayed*, *immediate*, and no prescribed antibiotics for clinical outcomes in the three studies that recruited participants with cough. For the outcome of fever with sore throat, three of the five studies favoured *immediate* antibiotics, and two found no difference. For the outcome of pain related to sore throat, two studies favoured *immediate* antibiotics, and three found no difference. One study compared *delayed* antibiotics with no antibiotic for sore throat, and found no difference in clinical outcomes.

Three studies included participants with acute otitis media. Of the two studies with an *immediate* antibiotic arm, one study found no difference for fever, and the other study favoured *immediate* antibiotics for pain and malaise severity on Day 3. One study including participants with acute otitis media compared *delayed* antibiotics with *no* antibiotics and found no difference for pain and fever on Day 3.

Two studies recruited participants with common cold. Neither study found differences for clinical outcomes between *delayed* and *immediate* antibiotic groups. One study favoured *delayed* antibiotics over *no* antibiotics for pain, fever, and cough duration (moderate quality evidence for all clinical outcomes - GRADE assessment).

There were either no differences for adverse effects or results favoured *delayed* antibiotics over *immediate* antibiotics (low quality evidence - to GRADE assessment) with no significant differences in complication rates.

Delayed antibiotics resulted in a significant reduction in antibiotic use compared to *immediate* antibiotics prescription (odds ratio (OR) 0.04, 95% confidence interval (CI) 0.03 to 0.05). However, a *delayed* antibiotic was more likely to result in reported antibiotic use than *no* antibiotics (OR 2.55, 95% CI 1.59 to 4.08) (moderate quality evidence - GRADE assessment).

Patient satisfaction favoured *delayed* over *no* antibiotics (OR 1.49, 95% CI 1.08 to 2.06). There was no significant difference in patient satisfaction between *delayed* antibiotics and *immediate* antibiotics (OR 0.65, 95% CI 0.39 to 1.10) (moderate quality evidence - GRADE assessment).

None of the included studies evaluated antibiotic resistance.

Authors' conclusions

For many clinical outcomes, there were no differences between prescribing strategies. Symptoms for acute otitis media and sore throat were modestly improved by *immediate* antibiotics compared with *delayed* antibiotics. There were no differences in complication rates. Delaying prescribing did not result in significantly different levels of patient satisfaction compared with immediate provision of antibiotics (86% versus 91%) (moderate quality evidence). However, delay was favoured over *no* antibiotics (87% versus 82%). *Delayed* antibiotics achieved lower rates of antibiotic use compared to *immediate* antibiotics (31% versus 93%) (moderate quality evidence). The strategy of *no* antibiotics further reduced antibiotic use compared to delaying prescription for antibiotics (14% versus 28%).

Delayed antibiotics for people with acute respiratory infection reduced antibiotic use compared to *immediate* antibiotics, but was not shown to be different to *no* antibiotics in terms of symptom control and disease complications. Where clinicians feel it is safe not to prescribe antibiotics immediately for people with respiratory infections, *no* antibiotics with advice to return if symptoms do not resolve is likely to result in the least antibiotic use while maintaining similar patient satisfaction and clinical outcomes to delaying prescription of antibiotics. Where clinicians are not confident in using a *no* antibiotic strategy, a *delayed* antibiotics strategy may be an acceptable compromise in place of *immediate* prescribing to significantly reduce unnecessary antibiotic use for RTIs, and thereby reduce antibiotic resistance, while maintaining patient safety and satisfaction levels.

Editorial note: As a living systematic review, this review is continually updated, incorporating relevant new evidence as it becomes available. Please refer to the Cochrane Database of Systematic Reviews for the current status of this review.

PLAIN LANGUAGE SUMMARY

Delayed antibiotic prescriptions for respiratory tract infections

Review question

We investigated the effect of *delaying* antibiotic prescription compared to *immediate* prescription or *no* antibiotics for people with respiratory tract infections including sore throat, middle ear infection, cough (bronchitis), and the common cold. We included all RTIs regardless of whether antibiotics were indicated or not. We also evaluated antibiotic use, patient satisfaction, antibiotic resistance, reconsultation rates, and use of supplemental therapies. This is an update of a review published in 2007, 2010, and 2013.

Background

Prescribing too many antibiotics increases the risk of adverse reactions and results in higher healthcare costs and increased antibacterial resistance.

One strategy to reduce unnecessary antibiotic prescribing is to provide an antibiotic prescription, but with advice to delay filling the prescription. The prescriber assesses that *immediate* antibiotics are not immediately required, expecting that symptoms will resolve without antibiotics.

Study characteristics

Evidence is current to 25th May 2017. We included 11 trials with a total of 3555 participants evaluating prescribing strategies for people with respiratory tract infections. Ten of these studies compared strategies of *delaying* antibiotics with *immediate* antibiotics. Four studies compared *delayed* antibiotics with *no* antibiotics. Of the 11 studies, five included only children (1173 participants), two included only adults (594 participants), and four included children and adults (1761 participants). The studies investigated a variety of respiratory tract infections. One study involving 405 participants was new for this update.

Key results

There were no differences between *immediate*, *delayed*, and *no* antibiotics for many symptoms including fever, pain, feeling unwell, cough, and runny nose. The only differences were small and favoured *immediate* antibiotics for relieving pain, fever, and runny nose for sore throat; and pain and feeling unwell for middle ear infections. Compared to *no* antibiotics, *delayed* antibiotics led to a small reduction in how long pain, fever, and cough persisted in people with colds. There was little difference in antibiotic adverse effects, and no significant difference in complications.

Patient satisfaction was similar for people who trialled *delayed* antibiotics (86% satisfied) compared to *immediate* antibiotics (91% satisfied), but was greater than *no* antibiotics (87% versus 82% satisfied). Antibiotic use was greatest in the *immediate* antibiotic group (93%), followed by *delayed* antibiotics (31%), and *no* antibiotics (14%).

In the first month after the initial consultation, two studies indicated that participants were no more likely to come back and see the doctor for *delayed* or *immediate* prescribing groups. Excluding the first month, one study found that participants were no more likely to return to see the doctor in the 12 months after the *delayed* or *immediate* prescription for another respiratory infection, and another study found that participants were more likely to come back and see the doctor in the next 12 months if they had had an *immediate* prescription compared to a *delayed* prescription.

Two studies including children with acute otitis media reported on the use of other medicines in *delayed* and *immediate* antibiotic groups. There was no difference in the use of ibuprofen, paracetamol, and otic drops in one study. In the other study, fewer spoons of paracetamol were used in the *immediate* antibiotic group compared with the *delayed* antibiotic group on the second and third day after the child's initial presentation. No included studies evaluated herbal or other forms of complementary medicine.

No included studies evaluated antibiotic resistance.

Quality of the evidence

Overall, the quality of the evidence was moderate according to GRADE assessment.

When doctors feel it is safe not to *immediately* prescribe antibiotics, advising *no* antibiotics but to return if symptoms do not resolve, rather than *delayed* antibiotics, will result in lower antibiotic use. However, patient satisfaction may be greater when a *delayed* prescribing strategy is used. Using a *delayed* antibiotic strategy will still result in a significant reduction in antibiotic use compared to the use of *immediate* antibiotics.

Editorial note: This is a living systematic review. Living systematic reviews offer a new approach to review updating in which the review is continually updated, incorporating relevant new evidence as it becomes available. Please refer to the Cochrane Database of Systematic Reviews for the current status of this review.