

Protective effect of antibiotics against serious complications of common respiratory tract infections: retrospective cohort study with the UK General Practice Research Database

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ABSTRACT

Objective To determine the extent to which antibiotics reduce the risk of serious complications after common respiratory tract infections.

Design Retrospective cohort study.

Setting UK primary care practices contributing to the general practice research database.

Data source 3.36 million episodes of respiratory tract infection.

Main outcome measures Risk of serious complications in treated and untreated patients in the month after diagnosis: mastoiditis after otitis media, quinsy after sore throat, and pneumonia after upper respiratory tract infection and chest infection. Number of patients needed to treat to prevent one complication.

Results Serious complications were rare after upper respiratory tract infections, sore throat, and otitis media, and the number needed to treat was over 4000. The risk of pneumonia after chest infection was high, particularly in elderly people, and was substantially reduced by antibiotic use, with a number needed to treat of 39 for those aged ≥ 65 and 96-119 in younger age groups.

Conclusion Antibiotics are not justified to reduce the risk of serious complications for upper respiratory tract infection, sore throat, or otitis media. Antibiotics substantially reduce the risk of pneumonia after chest infection, particularly in elderly people in whom the risk is highest.

INTRODUCTION

Recommendations not to prescribe antibiotics for common respiratory tract infections are based on concerns about the development of antimicrobial resistance and evidence from meta-analyses of randomised controlled trials that have shown minimal benefits.¹⁻⁴ Despite this, continuing high rates of prescribing may relate to patients' expectations and to fears about serious complications of infection.⁵ Research has suggested that low rates of antibiotic prescribing in primary care might be associated with higher rates of complications of infection.⁶⁻⁹ These studies cannot determine whether adverse events are occurring less frequently in those people who received antibiotics for minor infections than in those who did not. Meanwhile, randomised controlled trials generally have insufficient power to examine the effect of interventions on rare outcomes, and the patients included might not be representative of those seen in routine clinical practice.

We used a large primary care database to describe the effect of antibiotics in routine practice on the risk of

serious complications after common respiratory tract infections.

METHODS

We used data from 162 practices that contributed to the UK general practice research database from 1 July 1991 to 30 June 2001. In patients with common respiratory infections, we examined the risk of developing serious complications in the month after diagnosis of infection, excluding those that were recorded on the day of diagnosis. We calculated and compared this risk in those who were treated with antibiotics and those who were not. Patients were considered to have been prescribed an antibiotic for a respiratory tract infection if the prescription was issued on the day of the consultation. We included consultations for chest infection (excluding those in patients with a diagnosis of pneumonia at baseline), upper respiratory tract infection, sore throat, and acute otitis media based on OXMIS and Read codes (see bmj.com). Potentially serious complications were mastoiditis for otitis media, quinsy for sore throat, and pneumonia for chest infection and upper respiratory tract infection. In addition we examined the effect of antibiotics given for upper respiratory tract infection on the risk of chest infection in the subsequent month.

We used logistic regression, adjusted for age, sex, and social deprivation, to calculate odds ratios for the potential protective effect of antibiotics. Social deprivation was area based on Carstairs' scores. The analyses were further stratified on age if there was a significant interaction between age and antibiotic prescription.

RESULTS

The study included 1 081 000 episodes of upper respiratory tract infection, 1 065 088 cases of sore throat, and 459 876 cases of otitis media. The risk of serious complications in the month after diagnosis of these conditions was low and was significantly reduced with the use of antibiotics, but the number needed to treat to prevent one serious complication was over 4000 for all of these conditions (table). The protective effect of antibiotics did not vary significantly by age. The risk of a consultation for chest infection in the month after upper respiratory tract infection was 17 per 1000 in those not treated with antibiotics and 11 per 1000 in those who were treated (adjusted odds ratio 0.64, 95% confidence interval 0.58 to 0.71, number needed to treat = 161).

There were 749 389 episodes of chest infection. The risk of pneumonia in the month after diagnosis was

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high and was substantially reduced by antibiotics. This effect varied significantly with age, such that the greatest protective effect was in those aged 65 and over. Without an antibiotic prescription 4% of those aged 65 and over were diagnosed with pneumonia in the month after diagnosis of a chest infection compared with 1.5% of those who were treated with an antibiotic. The number needed to treat to prevent one diagnosis of pneumonia was 39 in this age group and 96-119 in younger age groups. Analyses stratified by smoking status and by underlying chronic respiratory disease found no evidence that these factors affected the risk of complications or the protective effect of antibiotics.

DISCUSSION

Principal findings of the study

The risk of serious complications after sore throat, otitis media, and upper respiratory tract infection is low and the number of courses of antibiotic needed to prevent one serious complication is high (over 4000). Antibiotics for upper respiratory tract infection reduced the risk of consultation for chest infection but even without treatment less than 2% of patients consulted with a chest infection in the following month. We found a substantial risk of pneumonia after chest infection, which was greatly reduced by antibiotic use, with a relatively low number of courses of antibiotic needed to prevent one diagnosis of pneumonia.

Strengths and weaknesses of the study

This was a large study of complications after common respiratory tract infections. The patients included in the study are probably highly representative of those seen in primary care. The cohort design allowed us to estimate the absolute risk of rare outcomes, the effect of antibiotics on this risk, and the number of antibiotic courses needed to prevent one complication. The non-randomised design means that it is likely that patients with more severe disease will be treated with antibiotics. If those with severe disease have a higher risk of complications then this would tend to lead to an underestimation of the protective effect of antibiotics.

In routine practice doctors are unlikely to apply strict case definitions when allocating diagnostic codes. For example, the term "chest infection" potentially includes both acute bronchitis and pneumonia,

only reliably distinguished by chest radiography (not readily available in primary care). See bmj.com. Several biases working in different directions may have influenced the findings, though they would need to be extreme to alter our main conclusions substantially.

Strengths and weaknesses in relation to other studies

Observational studies using large datasets of routinely collected primary care data are the only practicable way to examine the effect of antibiotic prescribing on rare complications of common infection. Randomised controlled trials could overcome some of the biases discussed but have insufficient power and are highly selective about the patients involved. Meta-analyses have had insufficient power to examine the protective effect of antibiotics for pneumonia after upper respiratory tract infection³ or for mastoiditis after otitis media.¹ With sample sizes of more than a million patients with upper respiratory tract infection (compared with 1495 participants in the meta-analysis)³ and nearly half a million with otitis media (compared with 1669 participants in the meta-analysis),⁴ we were able to show that, while antibiotics have a protective effect in these conditions, the number needed to treat to prevent complications is high.

Meta-analyses have shown that antibiotics can reduce the risk of quinsy after sore throat,² but this conclusion is primarily related to one large study in the 1950s, when the population incidence of quinsy was much higher than today.¹⁰ We included over a million cases of sore throat treated in the 1990s (compared with 10 101 participants included in the meta-analysis)² and showed that antibiotics do indeed reduce the risk of quinsy. As with upper respiratory tract infections and otitis media, however, the number needed to treat to prevent one serious complication is high.

Many less serious outcomes have previously been examined by randomised controlled trials and meta-analyses that have emphasised the minimal benefits of prescribing for upper respiratory tract infection, sore throat, and otitis media.¹⁻³ Antibiotics for upper respiratory tract infection did reduce the risk of consultations for chest infection in the following month but the number needed to treat (161) to prevent such a consultation was relatively high. This needs to be balanced against other research that has shown that prescribing

Protective effect of antibiotics for common respiratory tract infections and number needed to treat to prevent one complication

Infection/adverse outcome (age group)	Adjusted odds ratio* (95% CI)	Number needed to treat (95% CI)	P value
URTI/pneumonia	0.68 (0.58 to 0.79)	4407 (2905 to 9126)	<0.001
Otitis media/mastoiditis	0.56 (0.37 to 0.86)	4064 (2393 to 13 456)	0.008
Sore throat/quinsy	0.84 (0.73 to 0.97)	4300 (2522 to 14 586)	0.021
Chest infection/pneumonia (significant interaction between prescribing and age):			
0-4 years	0.22 (0.17 to 0.27)	101 (85 to 125)	<0.001
5-15 years	0.18 (0.13 to 0.24)	96 (73 to 137)	<0.001
16-64 years	0.27 (0.23 to 0.32)	119 (105 to 136)	<0.001
≥65 years	0.35 (0.33 to 0.38)	39 (36 to 42)	<0.001

URTI=upper respiratory tract infection.

*Adjusted for age, sex, and social deprivation.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Guidelines based on randomised controlled trials recommend that antibiotics should not be prescribed for upper respiratory tract infection, sore throat, or otitis media. Chest infections are divided into acute bronchitis (antibiotics not recommended) and pneumonia (antibiotics recommended).

WHAT THIS STUDY ADDS

Antibiotics reduce the risk of mastoiditis after otitis media, quinsy after sore throat, and pneumonia after upper respiratory tract infection but over 4000 courses of antibiotics are needed to prevent one complication. Conversely, the risk of pneumonia in those presenting with chest infection is high, particularly in elderly patients, and can be substantially reduced by the use of antibiotics.

for minor infections may make patients more likely to consult the next time they have such an infection.¹¹

We identified a higher risk of pneumonia after chest infection than observed in randomised control trials for treatment of acute bronchitis.⁴ In such trials care is taken to exclude pneumonia through use of chest radiography either for all patients or all those with focal chest signs. These procedures are likely to be less stringent in routine practice so our results are likely to be more pertinent to general practitioners' treatment decisions.

Implications of the study

There are legitimate concerns about the overuse of antibiotics in primary care and the development of resistance. A randomised controlled trial has shown increased carriage in resistant organisms after macrolide administration but not after placebo.¹²

Antibiotics substantially reduce the risk of a diagnosis of pneumonia after chest infection. Guidance emphasises the importance of a thorough clinical examination before the decision to withhold antibiotics from patients with chest infection. We have shown that antibiotic prescribing to reduce the risk of pneumonia after chest infection is justifiable, particularly in elderly patients.

Unanswered questions and future research

For upper respiratory tract infection, sore throat, and otitis media research should focus on effective interventions to reduce prescribing. For chest infection research should focus on developing clinical algorithms and diagnostic technology in primary care to enable confident distinction between acute bronchitis and early pneumonia and to identify those who are most likely to develop pneumonia.

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