Clinical pharmacology

Antibiotic prescribing in respiratory tract infections: first do no harm

The discovery of penicillin by Sir Alexander Fleming in 1928 ushered in the antibiotic era and transformed the practice of medicine. But the power of these life-saving drugs is waning as bacterial resistance to antibiotics is increasing. There is abundant evidence that over-prescribing of antibiotics is a major cause of resistance.[1,2] Patient expectations and demands for antibiotic treatment as well as the fear of serious infectious complications are key factors driving excessive antibiotic prescribing.[3] The treatment expectations of the patient seem to overrule our knowledge with regard to the dangers of excess antibiotic prescribing.[2]

Injudicious antibiotic prescribing also causes harm in the form of adverse drug reactions. Doctors are entrusted with the responsibility of *primum non nocere* or first to do no harm. Most respiratory tract infections seen in primary care are due to viruses, which do not respond to antibiotics. The few respiratory tract infections that are bacterial are largely self-limiting, so that the benefit of using antimicrobials is marginal. This article evaluates the benefits versus the risks of treating mild respiratory tract infections to illustrate how irrational prescribing of antibiotics can be detrimental to the individual.

Risk-benefit ratios

A clinician considering prescribing a drug should first evaluate the risk-benefit ratio. The evidence is not always available for all therapeutic decisions, partly because the reporting of harm caused by drugs is almost always less detailed than the reporting of benefits. The number needed to treat is the number of patients who have to be treated to benefit one patient. Benefits could vary from saving a life when evaluating treatments for myocardial infarctions to reducing days of cough for acute bronchitis. The number needed to harm is the number of patients that would need to receive the treatment to develop an adverse drug reaction. The larger the difference between the number needed to treat and the number needed to harm, the more favourable the risk-benefit ratio.

Evidence on number needed to treat and number needed to harm (if available) from systematic reviews of respiratory tract infections is presented graphically in Fig. 1.

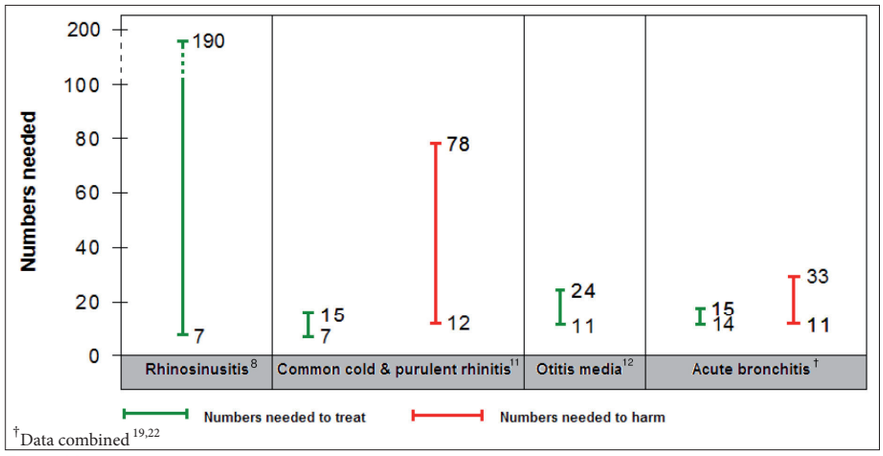

Fig. 1. Numbers needed to treat for symptomatic improvement of mild respiratory infections and numbers needed to harm (when available) for adverse drug reactions.

Risk of harm by not treating upper respiratory tract infections

Campaigns to reduce antibiotic prescribing for mild respiratory infections have been successful in several countries. Some clinicians have expressed concern that more conservative antibiotic use may result in more serious complications. The effect of antibiotics in preventing serious complications after common respiratory tract infections was examined in a recent study of 3.36 million consultations from the UK General Practice database.[4] Patients treated with and without antibiotics for common respiratory infections were compared. Patients were reviewed after the diagnosis of the initial respiratory tract infection to deter-mine whether any complications ensued within the following month. Complications evaluated were pneumonia, quinsy and mastoiditis. Antibiotics significantly reduced these complications, but the number of patients with the relevant respiratory tract infection needed to treat to prevent each of these serious complications was over 4 000.

Risk of harm from antibiotics

What is the incidence of adverse drug reactions from antibiotics? For every 10 000 outpatient antibiotic prescriptions, 10.5 patients will present to an emergency department with an adverse event due to an antibiotic (95% CI, 8.3 - 12.6).[5] Penicillins and cephalosporins were implicated in more than half of the estimated emergency department visits for antibiotic-associated adverse events. Infants younger than 1 year had the highest frequency of adverse events attributable to antibiotics. In other words, in order to prevent 1 serious complication of common respiratory tract infections, more than 4 000 antibiotic scripts need to be dispensed, but for every 1 000 scripts at least 1 patient will experience an antibiotic adverse event serious enough for the patient to present to an emergency department.

The rate of emergency department visits for antibiotic-associated adverse events is half the rate of emergency department visits for adverse events caused by the high-risk medications warfarin, insulin and digoxin (20.6 emergency department visits per 10 000 outpatient prescription visits).[6] This clearly demonstrates that antibiotics are not the harmless better-safe-than-sorry drug they are perceived to be. Furthermore, an analysis focused only on emergency department visits does not reflect all adverse events due to antibiotics, which will be considerably higher.

Risk-benefit ratios for upper respiratory tract infections

Health-related quality of life is not significantly improved in patients receiving antibiotics for an upper respiratory tract infection when compared with subjects receiving no antibiotic.[7] Deciding which patients with upper respiratory tract infections need antibiotic treatment is complex. Some guidelines are given below. In addition, it is prudent to be more aggressive with vulnerable patients, such as diabetics and the HIV-infected.

Rhinosinusitis

A recent meta-analysis found that 15 adults with rhinosinusitis-like complaints need to be treated with an antibiotic to cure 1 patient, and 64% of patients are cured after 14 days without antibiotic treatment.[8] With the exception of purulent discharge in the pharynx that had some prognostic value (8 patients with this sign needed to be treated before 1 patient was cured), common clinical

signs and symptoms failed to identify patients in whom antibiotic treatment was justified. It should be noted that the trials in this meta-analysis excluded patients with high fever, periorbital swelling, erythema or intense facial pain that suggest a serious complication and warrant antibiotic cover. The number needed to harm for an antibiotic adverse event was 12 - 78 patients in another meta-analysis.[9] Patients treated with antibiotics for rhinosinusitis report a twofold increased risk of diarrhoea compared with placebo.[10] The Cochrane meta-analysis for common cold and acute purulent rhinitis concluded that antibiotics have no benefit in the treatment but has a more than double risk for adverse events.[11]

Otitis media

The Cochrane meta-analysis of otitis media in children found that 15 children needed to be treated with antibiotics in order to prevent 1 child from experiencing pain after 2 - 7 days, with no significant difference in hearing or other complications compared with placebo. Once again the risk of adverse events was nearly double in the children treated with antibiotics.[12] Many international guidelines therefore recommend treating symptomatically and deferring antibiotics for the first 48 hours, except for children younger than 2 years, who benefit more from antibiotics than older children.

Sore throat

Due to the high prevalence of rheumatic fever in our population, the South African guideline recommends empirical treatment for suspected streptococcal throat infections in children aged 3 - 15 years.[13] The number needed to treat to prevent 1 case of rheumatic fever is 53 with oral penicillin and 60 with intramuscular penicillin.[14] The absolute benefit of antibiotics for the duration of sore throat symptoms is modest, with a reduction of symptoms of about 1 day.[15]

Lower respiratory tract infections

In patients with chest infections, the risk of pneumonia in the month after diagnosis is reduced by antibiotics.[4] This effect varied significantly with age and the greatest protective effect was in those aged 65 and over. The number needed to treat to prevent pneumonia was 39 in the older age group and between 96 and 119 in younger age groups. In acute bronchitis the modest benefit of treating may be outweighed by the cost, adverse effects and negative consequences on antibiotic resistance.[16] Antibiotics decrease the duration of cough in acute bronchitis by only 0.58 days.[16]

Changing the culture of antibiotic prescribing

Practitioners spend significantly less time with a patient when they prescribe an antibiotic for a respiratory tract infection.[17] It is less time consuming to write a script than to explain to patients why antibiotics are not necessary. Concepts of antibiotic resistance and benefit versus risk are difficult to explain to patients. Antibiotic use is greater among patients believing that antibiotics are effective for both viral and bacterial illnesses and education of patients is an important component of intervention in respiratory tract infections.[18] Using benign-sounding labels such as a chest cold when a patient presents with an acute bronchitis, may not affect patient satisfaction but may improve satisfaction by not prescribing an antibiotic.[19] Patients' expectations are seldom explicit and satisfaction is not necessarily related to receiving an antibiotic. Providing disease information and reassurance might be more valuable.[20] Even when antibiotics are indicated for lower respiratory tract infections, doctors are dismal at adhering to local guidelines.[21]

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In a nutshell

- The risk-benefit ratio of antibiotics for upper respiratory tract infections is marginal.
- The number needed to treat to prevent 1 serious complication after an upper respiratory tract infection is over 4 000 while the number needed to cause an adverse event due to antibiotic use is 1 000.
- The lower respiratory tract infection risk-benefit ratio is more favourable in the elderly.
- It is less time consuming for practitioners to write a script than to explain to patients why antibiotics are not necessary.