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[Intervention Review]

Prolonged antibiotics for non-cystic fibrosis bronchiectasis in children and adults

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ABSTRACT

Background

The vicious cycle hypothesis for bronchiectasis predicts that bacterial colonisation of the respiratory tract perpetuates inflammatory change. This damages the mucociliary escalator, preventing bacterial clearance and allowing persistence of pro-inflammatory mediators. Conventional treatment with physiotherapy and intermittent antibiotics is believed to improve the condition of people with bronchiectasis, although no conclusive data show that these interventions influence the natural history of the condition. Various strategies have been tried to interrupt this cycle of infection and inflammation, including prolonging antibiotic treatment with the goal of allowing the airway mucosa to heal.

Objectives

To determine the benefits of prolonged antibiotic therapy in the treatment of patients with bronchiectasis.

Search methods

We searched the Cochrane Airways Group Trials Register and reference lists of identified articles. Searches were current as of February 2014.

Selection criteria

Randomised trials examining the use of prolonged antibiotic therapy (for four or more weeks) in the treatment of bronchiectasis compared with placebo or usual care.

Data collection and analysis

Two review authors independently assessed trial quality and extracted data. We contacted study authors to ask for missing information.

Main results

Eighteen trials met the inclusion criteria, randomly assigning a total of 1157 participants. Antibiotics were given for between four weeks and 83 weeks. Limited meta-analysis was possible because of the diversity of outcomes reported in these trials. Based on the number of participants with at least one exacerbation, the meta-analysis showed significant effects in favour of the intervention (odds ratio (OR) 0.31, 95% confidence interval (CI) 0.19 to 0.52; P value < 0.00001), with events occurring in 271 per 1000 people in the intervention arm (95% CI 126 to 385) and in 546 per 1000 in the control population, based on evidence of moderate quality. A non-statistically significant reduction in hospitalisation favoured the use of prolonged antibiotics with a moderate quality grade of supporting evidence (37 per 1000

in the intervention arm (95% CI 13 to 96) and 87 per 1000 in control (OR 0.40, 95% CI 0.14 to 1.11; P value = 0.08). Drug resistance developed in 36 of 220 participants taking antibiotics compared with 10 of 211 participants given placebo or standard therapy (OR 3.48, 95% CI 1.20 to 10.07; P value = 0.02), translating to natural frequencies of 155 per 1000 in the intervention arm (95% CI 59 to 346) and 50 per 1000 in the control arm. The intervention was well tolerated with no overall significant difference in withdrawal between treatment and placebo groups (OR 0.91, 95% CI 0.56 to 1.49). Diarrhoea was commonly reported as an adverse event, particularly with an oral intervention.

Authors' conclusions

Available evidence shows benefit associated with use of prolonged antibiotics in the treatment of patients with bronchiectasis, at least halving the odds of exacerbation (with 275 fewer exacerbations per every 1000 people treated in the antibiotic arm compared with the control arm) and hospitalisation (50 fewer hospitalisations per 1000 people in the antibiotic arm compared with the control arm). However, the risk of emerging drug resistance is increased more than threefold. This review is limited by diversity of trials and by evidence of moderate to low quality. Further randomised controlled trials with adequate power and standardised end points are required.

PLAIN LANGUAGE SUMMARY

Prolonged antibiotics for purulent bronchiectasis in children and adults

Does prolonged antibiotic therapy provide benefit in treatment of patients with purulent bronchiectasis?

Why is this question important?

Non-cystic fibrosis (CF) bronchiectasis is a chronic respiratory condition characterised by abnormal dilatation of the airways. Although its global prevalence is largely unknown, available data from Australia, New Zealand, the United States and England show that bronchiectasis is now diagnosed with increasing frequency. The lungs of patients with bronchiectasis have excessive secretions, which tend to consist of different types of micro-organisms. Long-term antibiotic therapy was proposed to halt persistent and ongoing damage to the lung due to insult from micro-organisms. Therefore, we seek to assess the effects of prolonged antibiotic therapy on patients with bronchiectasis.

How did we answer the question?

We looked for all studies comparing prolonged antibiotic therapy versus usual care and/or a dummy medication (placebo).

What did we find?

We found 18 studies including 1157 people with non-cystic fibrosis bronchiectasis; most were adults. Twelve studies used a tablet form of antibiotics (e.g. azithromycin, erythromycin, roxithromycin, amoxycillin, clarithromycin, penicillin, oxytetracycline, ciprofloxacin). The remaining six studies reported use of inhaled medications. Antibiotics were given for between four weeks and 83 weeks. In seven studies, similar disease severity at baseline was supported by the similar history of previous hospitalisation and severe attacks.

Overall quality of evidence was rated as moderate. When an outcome is rated as high quality, further research is very unlikely to change our confidence in the estimate of effect, but moderate ratings reflect some uncertainty in the findings.

Conclusion

Prolonged antibiotic therapy in bronchiectasis provides benefit, especially in reducing the risk of future exacerbations and hospitalisations. Antibiotics are well tolerated by participants without significant differences in overall adverse effects (e.g. intolerance, chest symptoms, fatigue, fever, palpitations).

However, antibiotic resistance is a matter of concern, particularly for patients with drug allergies, which further limit their future treatment.