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[Intervention Review]

Dual antibiotics for bronchiectasis

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ABSTRACT

Background

Bronchiectasis is a chronic respiratory disease characterised by abnormal and irreversible dilatation of the smaller airways and associated with a mortality rate greater than twice that of the general population. Antibiotics serve as front-line therapy for managing bacterial load, but their use is weighed against the development of antibiotic resistance. Dual antibiotic therapy has the potential to suppress infection from multiple strains of bacteria, leading to more successful treatment of exacerbations, reduced symptoms, and improved quality of life. Further evidence is required on the efficacy of dual antibiotics in terms of management of exacerbations and extent of antibiotic resistance.

Objectives

To evaluate the effects of dual antibiotics in the treatment of adults and children with bronchiectasis.

Search methods

We identified studies from the Cochrane Airways Group Specialised Register (CAGR), which includes the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), Allied and Complementary Medicine (AMED), and PsycINFO, as well as studies obtained by handsearching of journals/abstracts. We also searched the following trial registries: US National Institutes of Health Ongoing Trials Register, ClinicalTrials.gov, and the World Health Organization (WHO) International Clinical Trials Registry Platform. We imposed no restriction on language of publication. We conducted our search in October 2017.

Selection criteria

We searched for randomised controlled trials comparing dual antibiotics versus a single antibiotic for short-term (< 4 weeks) or long-term management of bronchiectasis diagnosed in adults and/or children by bronchography, plain film chest radiography, or high-resolution computed tomography. Primary outcomes included exacerbations, length of hospitalisation, and serious adverse events. Secondary outcomes were response rates, emergence of resistance to antibiotics, systemic markers of infection, sputum volume and purulence, measures of lung function, adverse events/effects, deaths, exercise capacity, and health-related quality of life. We did not apply outcome measures as selection criteria.

Data collection and analysis

Two review authors independently screened the titles and abstracts of 287 records, along with the full text of seven reports. Two studies met review inclusion criteria. Two review authors independently extracted outcome data and assessed risk of bias. We extracted data from



only one study and conducted GRADE assessments for the following outcomes: successful treatment of exacerbation; response rates; and serious adverse events.

Main results

Two randomised trials assessed the effectiveness of oral plus inhaled dual therapy versus oral monotherapy in a total of 118 adults with a mean age of 62.8 years. One multi-centre trial compared inhaled tobramycin plus oral ciprofloxacin versus ciprofloxacin alone, and one single-centre trial compared nebulised gentamicin plus systemic antibiotics versus a systemic antibiotic alone. Published papers did not report study funding sources.

Effect estimates from one small study with 53 adults showed no evidence of treatment benefit with oral plus inhaled dual therapy for the following primary outcomes at the end of the study: successful management of exacerbation - cure at day 42 (odds ratio (OR) 0.66, 95% confidence interval (CI) 0.22 to 2.01; 53 participants; one study; very low-quality evidence); number of participants with *Pseudomonas aeruginosa* eradication at day 21 (OR 2.33, 95% CI 0.66 to 8.24; 53 participants; one study; very low-quality evidence); and serious adverse events (OR 0.48, 95% CI 0.08 to 2.87; 53 participants; one study; very low-quality evidence). Similarly, researchers provided no evidence of treatment benefit for the following secondary outcomes: clinical response rates - relapse at day 42 (OR 0.57, 95% CI 0.12 to 2.69; 53 participants; one study; very low-quality evidence); microbiological response rate at day 21 - eradicated (OR 2.40, 95% CI 0.67 to 8.65; 53 participants; one study; very low-quality evidence); and adverse events - incidence of wheeze (OR 5.75, 95% CI 1.55 to 21.33). Data show no evidence of benefit in terms of sputum volume, lung function, or antibiotic resistance. Outcomes from a second small study with 65 adults, available only as an abstract, were not included in the quantitative data synthesis. The included studies did not report our other primary outcomes: duration; frequency; and time to next exacerbation; nor our secondary outcomes: systemic markers of infection; exercise capacity; and quality of life. We did not identify any trials that included children.

Authors' conclusions

A small number of studies in adults have generated high-quality evidence that is insufficient to inform robust conclusions, and studies in children have provided no evidence. We identified only one dual-therapy combination of oral and inhaled antibiotics. Results from this single trial of 53 adults that we were able to include in the quantitative synthesis showed no evidence of treatment benefit with oral plus inhaled dual therapy in terms of successful treatment of exacerbations, serious adverse events, sputum volume, lung function, and antibiotic resistance. Further high-quality research is required to determine the efficacy and safety of other combinations of dual antibiotics for both adults and children with bronchiectasis, particularly in terms of antibiotic resistance.

PLAIN LANGUAGE SUMMARY

Dual antibiotics for bronchiectasis

Background to the question

Bronchiectasis is a lung disease involving abnormal airways, leading to repeated chest infections, and associated with a mortality rate more than twice that of the general population. Although previously considered a relatively rare disease, numbers appear to be increasing, particularly for those over 75 years in low/middle-income countries. Antibiotics are the main therapy for chest infection, but their use must be weighed against potential side effects and the risk of increasing resistance to antibiotic therapy. One strategy to improve response and/or reduce antibiotic resistance involves giving two antibiotic agents at the same time: dual antibiotic therapy. This review therefore aimed to evaluate the effects of dual antibiotics for treatment of adults and children with bronchiectasis.

Study characteristics

In October 2017, we identified two relevant studies comparing oral plus inhaled dual therapy versus oral therapy alone. They included a total of 118 adults with an average age of 62.8 years. One study compared inhaled tobramycin plus oral ciprofloxacin with oral ciprofloxacin, and the second study compared inhaled gentamicin plus a systemic (affecting the whole body, rather than just the lungs) antibiotic with a systemic antibiotic alone. Only a research summary was available for the latter. Published papers did not report study funding sources

Main results

Results from one small trial of 53 adults show no evidence of treatment benefit with oral plus inhaled dual therapy in terms of successful treatment of exacerbations, the occurrence of serious unwanted events, amount of phlegm, lung function, or resistance to antibiotic treatment. However, we found insufficient evidence to permit confident conclusions about their use.

Quality of the evidence

The overall quality of the evidence was very poor, largely because one of the studies was not well described and included few participants. Information on exacerbations, exercise ability, and quality of life was not reported. We did not identify any trials that compared other types of dual antibiotic therapy, and we found none that included children. Therefore uncertainty remains concerning the use of dual antibiotics, and further high-quality studies are needed to examine the role of dual antibiotics in the treatment of adults and children with bronchiectasis.