Antibiotics for exacerbations of chronic obstructive pulmonary disease (Review)

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Antibiotics for exacerbations of chronic obstructive pulmonary disease

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ABSTRACT

Background

Many patients with an exacerbation of chronic obstructive pulmonary disease (COPD) are treated with antibiotics. However, the value of antibiotics remains uncertain as systematic reviews and clinical trials have shown conflicting results.

Objectives

To assess the effects of antibiotics in the management of acute COPD exacerbations on treatment failure as observed between seven days and one month after treatment initiation (primary outcome) and on other patient-important outcomes (mortality, adverse events, length of hospital stay).

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE and other electronically available databases up to September 2012.

Selection criteria

Randomised controlled trials (RCTs) in people with acute COPD exacerbations comparing antibiotic therapy and placebo with a follow-up of at least seven days.

Data collection and analysis

Two review authors independently screened references and extracted data from trial reports. We kept the three groups of outpatients, inpatients and patients admitted to the intensive care unit (ICU) separate for benefit outcomes and mortality because we considered them to be clinically too different to be summarised in one group. We considered outpatients to have a mild to moderate exacerbation, inpatients to have a severe exacerbation and ICU patients to have a very severe exacerbation. Where outcomes or study details were not reported we requested missing data from the authors of the primary studies. We calculated pooled risk ratios (RR) for treatment failure, Peto odds ratios (OR) for rare events (mortality and adverse events) and weighted mean differences (MD) for continuous outcomes using fixed-effect models. We used GRADE to assess the quality of the evidence.
Main results

Sixteen trials with 2068 participants were included. In outpatients (mild to moderate exacerbations), there was evidence of low quality that antibiotics did statistically significantly reduce the risk for treatment failure between seven days and one month after treatment initiation (RR 0.75; 95% CI 0.60 to 0.94; $I^2 = 35\%$) but they did not significantly reduce the risk when the meta-analysis was restricted to currently available drugs (RR 0.80; 95% CI 0.63 to 1.01; $I^2 = 33\%$). Evidence of high quality showed that antibiotics statistically significantly reduced the risk of treatment failure in inpatients with severe exacerbations (ICU not included) (RR 0.77; 95% CI 0.65 to 0.91; $I^2 = 47\%$) regardless of whether restricted to current drugs. The only trial with 93 patients admitted to the ICU showed a large and statistically significant effect on treatment failure (RR 0.19; 95% CI 0.08 to 0.45; high-quality evidence).

Evidence of low-quality from four trials in inpatients showed no effect of antibiotics on mortality (Peto OR 1.02; 95% CI 0.37 to 2.79). High-quality evidence from one trial showed a statistically significant effect on mortality in ICU patients (Peto OR 0.21; 95% CI 0.06 to 0.72). Length of hospital stay (in days) was similar in the antibiotics and placebo groups except for the ICU study where antibiotics statistically significantly reduced length of hospital stay (mean difference -9.60 days; 95% CI -12.84 to -6.36 days). One trial showed no effect of antibiotics on re-exacerbations between two and six weeks after treatment initiation. Only one trial (N = 35) reported health-related quality of life but did not show a statistically significant difference between the treatment and control group.

Evidence of moderate quality showed that the overall incidence of adverse events was higher in the antibiotics groups (Peto OR 1.53; 95% CI 1.03 to 2.27). Patients treated with antibiotics experienced statistically significantly more diarrhoea based on three trials (Peto OR 2.62; 95% CI 1.11 to 6.17; high-quality evidence).

Authors’ conclusions

Antibiotics for COPD exacerbations showed large and consistent beneficial effects across outcomes of patients admitted to an ICU. However, for outpatients and inpatients the results were inconsistent. The risk for treatment failure was significantly reduced in both inpatients and outpatients when all trials (1957 to 2012) were included but not when the analysis for outpatients was restricted to currently used antibiotics. Also, antibiotics had no statistically significant effect on mortality and length of hospital stay in inpatients and almost no data on patient-reported outcomes exist. These inconsistent effects call for research into clinical signs and biomarkers that help identify patients who benefit from antibiotics and patients who experience no effect, and in whom downsides of antibiotics (side effects, costs and multi-resistance) could be avoided.

Plain language summary

Antibiotics for exacerbations of chronic obstructive pulmonary disease

Chronic obstructive pulmonary disease (COPD) is a chronic condition, often caused by smoking, which affects the passage of air in and out of the lungs. Exacerbations of COPD are defined as a sustained worsening of the patient’s symptoms from their usual stable state and commonly reported symptoms are worsening breathlessness, cough, increased sputum production and change in sputum colour. Antibiotics are frequently prescribed for exacerbations in patients with COPD although the cause of exacerbations is often difficult to determine (viral, bacterial, environmental). We did this systematic review to find out if there is good evidence for using antibiotics for exacerbations of COPD and if benefits of taking antibiotics in individuals outweigh potential harms for individual patients and the risks of multi-resistant bacteria to the population.

We found 16 randomised studies compared antibiotics with placebo in a total of 2068 COPD patients who presented with a wide range of severities of exacerbations. Analyses showed that antibiotics reduce treatment failures (no improvement) compared with placebo in hospitalised patients with severe exacerbations. In outpatients with mild to moderate exacerbations, the evidence is more unclear because analyses showed a reduction of treatment failure when all studies and antibiotics were considered, but analyses did not suggest such an effect when they were restricted to antibiotics in current use. Length of hospital stay and mortality were not reduced by antibiotics in hospitalised patients except for those who needed treatment on the intensive care unit. Patients treated with antibiotics experienced diarrhoea twice as often as patients receiving placebo. Severity of underlying COPD could not be compared across trials because lung function and other parameters were reported inconsistently between trials.

Current evidence shows that antibiotics reduce treatment failures in patients who are hospitalised for the treatment of a COPD exacerbation, and to a lesser extent in outpatients. Mortality is only reduced by antibiotics in patients with very severe exacerbations who need treatment in the intensive care unit. The rather small and inconsistent effects of antibiotics on treatment failure suggest that antibiotics are effective in some patients but not in all inpatients and outpatients. Future high-quality studies should explore how
antibiotic therapy may be targeted towards patients who benefit by using clinical signs (e.g. purulent sputum) or biomarkers at the time when patients present to the primary care doctor or emergency department.