Antibiotic treatment of acute bronchitis in smokers: a systematic review

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Authors' objectives
To determine the efficacy of antibiotics for smokers with acute bronchitis.

Searching
MEDLINE was searched from January 1966 to September 2001 for English language articles. The search terms were reported. The references of retrieved articles were checked for additional studies.

Study selection

Study designs of evaluations included in the review
Randomised placebo-controlled trials were eligible.

Specific interventions included in the review
Studies of antibiotics were eligible. The antibiotics examined in the included trials were doxycycline, trimethoprim-sulfamethoxazole (TMP-SMX) and erythromycin.

Participants included in the review
Studies of adults with acute bronchitis, both smokers and nonsmokers, who were previously healthy, were eligible. Acute bronchitis was defined as a productive cough of less than a month's duration in a patient without a history of cardiac or pulmonary disease and with no clinical signs of pneumonia. Patients could have rhonchi or wheezes on auscultation. Studies of patients with acute exacerbation of chronic bronchitis were excluded. Where stated, the proportion of smokers in the included studies ranged from 32 to 75% and the mean age of the patients ranged from 30 to 43 years.

Outcomes assessed in the review
The authors did not specify any inclusion criteria relating to the outcomes. The outcome measures used in the included studies were duration of cough, duration of yellow sputum, time off work, activity level, symptom scores, physician assessment and duration of fever.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The validity of the included studies was assessed using the method of Jadad et al., which gives a score out of 5 based on randomisation, blinding and withdrawals. The authors did not state how the papers were assessed for validity, or how many reviewers performed the validity assessment.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. The data extracted from the included studies included information relating to the main outcomes, and data to calculate the point estimates and 95% confidence intervals for the mean difference in duration or score for continuous outcomes in all patients using a two-sample t-test. Data were not available to do this for smokers only. Data on adverse effects were also extracted, and Fisher's exact test was used to compare antibiotics with placebo.

Methods of synthesis
How were the studies combined?
A narrative synthesis of the studies was undertaken. Available information specific to smokers was highlighted.

How were differences between studies investigated?
Differences between the studies were not investigated.

Results of the review
Nine randomised trials (total n=774, including over 276 smokers) were included.

No studies specifically addressed antibiotic use in smokers or reported subgroup data for smokers. The results for smokers were as reported by the original study authors.

The mean quality score was 3.9 (range: 3 to 5) out of a maximum of 5, indicating some deficiencies in blinding, randomisation or follow-up.

Antibiotics showed no overall benefit in five of the trials. In four of these trials, smoking status did not alter the lack of response to antibiotics, with one trial showing a trend towards reduced symptom scores only among nonsmokers receiving erythromycin and a trend toward higher symptom scores among smokers receiving erythromycin. One trial did not stratify by smoking status.

In another trial, TMP-SMX resulted in less frequent cough over 7 days in all patients treated (93% for TMP-SMX treated group versus 99% in placebo treated group; one-tailed P=0.05), but not among smokers.

The remaining three trials reported decreased duration of daytime cough, days off work, and sputum production score for antibiotic-treated patients. For all three trials, smoking status neither enhanced nor diminished the patients' response to antibiotics.

In the seven trials where they were reported, adverse effects averaged 11% (range among trials: 0 to 37) in placebo-treated patients and 16% (range among trials: 6 to 36) in antibiotic-treated patients (P=0.08). The most frequent adverse effects were gastrointestinal upset, nausea and vomiting. No trial stratified adverse effects by smoking status.

Authors' conclusions
The existing data indicated that any benefit to smokers with acute bronchitis from antibiotics was similar, or less, than for nonsmokers.

CRD commentary
The objective of the review was clear and the inclusion criteria relating to the interventions, participants and study design were appropriate. The authors did not specify a priori inclusion criteria for the outcomes, therefore selective reporting is a possibility. One database was searched for English language studies, and the authors did not report any specific attempt to identify unpublished studies. Thus, it is possible that relevant studies could have been missed and that the findings might be influenced by publication and language bias. The quality of the included studies was appropriately assessed and study details were reported. The authors did not provide details of the original results of the included studies before the data were transformed to point estimates. A narrative synthesis was appropriate, although differences between the studies were not adequately investigated. The authors did not specify any details of how the review was conducted, so it is not possible to determine whether steps were taken to minimise bias in the review process. The most tentative interpretation of the authors' conclusions is advisable.

Implications of the review for practice and research
Practice: The authors stated that smokers should use symptomatic treatment and avoid antibiotics for acute bronchitis.

Research: The authors stated that further trials are required in smokers with acute bronchitis to determine whether antibiotics are more useful in such a group than in nonsmokers. The authors stated that such trials should have well-defined inclusion criteria, sufficient power to detect meaningful clinical differences between the groups, and validated
outcome measures.

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