Short- versus long-course antibacterial therapy for community-acquired pneumonia: a meta-analysis

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CRD summary
This review concluded that there was no difference in the effectiveness and safety of short- versus long-course antimicrobial treatment for adult and paediatric patients with mild to moderate community-acquired pneumonia. The authors' conclusions reflect the evidence presented, but should not be considered definitive given the small number of trials in the analysis.

Authors' objectives
To assess the effectiveness and safety of using shorter than traditionally recommended antibacterial therapy for community-acquired pneumonia.

Searching
MEDLINE and Cochrane Register of Controlled Trials (CENTRAL) were searched up to November 2007; search terms were reported. References of relevant articles were scanned. Only articles in English, French, Spanish, German, Italian and Greek were included.

Study selection
Randomised controlled trials (RCTs) that compared the same antibacterial regimens in the same doses, but with one arm having a short course of treatment (seven days maximum) and one arm with a long course of treatment (at least two days longer than the short course) were eligible for inclusion. Patients of all ages (except neonates) were included provided that they had a diagnosis of community acquired pneumonia of any severity, based on at least two types of criteria (clinical, radiological and microbiological). Eligible trials were required to report one of the outcomes of interest.

The primary effectiveness outcome of interest was clinical success, defined as complete resolution or improvement of symptoms and signs of community-acquired pneumonia, assessed at the end of therapy evaluation visit. The primary safety outcome was the total number of adverse events that occurred by the end of the follow-up period. The other outcomes of interest were clinical success at the late follow-up evaluation visit, microbiological success, mortality, and relapse and withdrawals due to adverse events (definitions provided for all outcomes).

The included trials were of adults only or children only. The included children were aged two to 59 months old, with non-severe community-acquired pneumonia and resided in developing countries. The included adults were treated as in-patients or out-patients and none required admission to an intensive care unit; however, the severity of disease was unclear in several trials. The therapies used were gemifloxacin (five versus seven days); amoxicillin (three versus eight days; three versus five days); telithromycin (five versus seven days); ceftriaxone (five versus 10 days); and cefuroxime axetil (seven versus 10 days). The timing for end of therapy evaluation ranged from six to 21 days and from 12 to 45 days for late follow-up.

The authors did not state how many reviewers were involved in study selection.

Assessment of study quality
Trial were assessed for description of randomisation, blinding and reporting of withdrawals using the Jadad criteria. The maximum possible score was 5 points; trials with more than 2 points were considered to be of adequately good quality.

The authors did not state how many reviewers assessed quality.
Data extraction
Data on the number of events for each outcome and the number of evaluable patients (i.e. patients for whom outcome data were available) were extracted and the odds ratio (OR) and 95% confidence interval (CI) calculated.

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
Pooled odds ratio and 95% confidence intervals were estimated using a Mantel-Haenszel fixed-effect model where statistically significant heterogeneity was not observed; otherwise the DerSimonian-Laird random-effects model was used. Trials of adults and children were pooled separately and together. Heterogeneity was assessed using the $X^2$ test; a p-value of less than 0.1 was defined as statistically significant heterogeneity.

Publication bias was assessed using the Egger test.

Results of the review
Seven double-blind RCTs were included in the review. All had a quality score of at least 4 points, meeting the criteria for adequately good quality.

There was no difference between short- and long-course regimens for the primary effectiveness outcome of clinical success at end of therapy follow-up (OR 0.89, 95% CI 0.74 to 1.07; six RCTs; 5,107 patients) or the primary safety outcome of number of adverse events at the last follow-up (OR 0.90, 95% CI 0.72 to 1.13; five RCTs; 3,214 patients).

There was no difference between short- and long-course regimens for the secondary outcomes of clinical success at late follow-up (four RCTs); microbiological success (three RCTs); relapse rate (three RCTs) and withdrawals due to adverse events (six RCTs).

There were no between group differences for adult and child subgroups for mortality, although the number of deaths was small (one in the trials of children and 16 in the adult trials); these results were consistent with the results from the overall pooling.

There was no statistically significant heterogeneity.

Authors’ conclusions
There was no difference in the effectiveness and safety of short- versus long-course antimicrobial treatment of adult and child with mild to moderate severity community-acquired pneumonia.

CRD commentary
The review had clearly stated inclusion criteria. Two relevant databases were searched and studies in several languages were included. However, some relevant studies may have been missed in other languages and unpublished studies were not specifically sought. It was unclear whether appropriate methods were used to reduce error and bias in the study selection, quality assessment and data extraction.

Trial quality was assessed, but the adequacy of treatment allocation did not appear to be considered. Relevant study details were reported. The analysis seemed appropriate and took into consideration clinical and statistical heterogeneity, although a sensitivity analysis examining the impact of including only evaluable patients in the analysis, rather than an analysis based on all patients, would have been useful. The generalisability of the findings was considered; the authors stated that caution should be taken in extrapolating the findings to non-ambulatory patients with moderate to severe disease.

Overall, the authors’ conclusions reflect the evidence presented, but they should not be considered definitive given the small number of trials in the analysis (as highlighted by the authors) and the unclear reliability of some aspects of the review process (which were not reported).
Implications of the review for practice and research

**Practice**: The authors suggested that a shorter duration of antimicrobial therapy should be particularly considered for patients who rapidly respond to initially administered antimicrobial regimens, but that further research is required before definite recommendations can be made.

**Research**: The authors stated that further research is required that includes sicker patients, where disease severity is assessed using appropriate scores, and also to investigate whether similar effects are obtained with combination regimens.

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