Antibacterial class is not obviously important in outpatient pneumonia: a meta-analysis

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CRD summary
This review assessed whether improved clinical and mortality outcomes are achieved for outpatient community acquired pneumonia treated with antibacterials with coverage against atypical organisms. The authors concluded that there was no evidence of superiority for any drug comparison. Given some methodological uncertainties identified in the review process, the extent to which this conclusion was reliable was unclear.

Authors' objectives
To compare outcomes between different antibiotic classes in treating outpatient-treated community acquired pneumonia (OCAP).

Searching
MEDLINE (1966-2007) and EMBASE (1980-2007) were searched to identify relevant articles for inclusion in the review. Searches of the ACP Journal Club, Cochrane Controlled Trials Register, Cochrane Database of Systematic Reviews and DARE were undertaken for evidence-based reviews. Search terms were reported. The reference lists of retrieved articles, guidelines and review articles were searched for additional studies. The search was restricted to English-language studies.

Study selection
Randomised double-blind trials that compared antibacterial classes in adult (18 years or over) OCAP were eligible for inclusion. Studies that combined inpatients and outpatients were excluded, as were open-label, non-comparative and non-randomised studies. The included studies assessed the following oral therapies at differing doses: fluoroquinolones (moxifloxacin, sparflloxacin, levoflaxacin, grepafloxacin, trovafloxacin); macrolides (clarithromycin, azithromycin, roxitromycin); cephalosporins (cefaclor, cefixime, cefidoren, cefuroxime); and penicillin (amoxicillin/clavulanate). Study duration ranged from five to 14 days. The mean age of the patients was 49 years and 53 per cent were male. The primary outcomes of interest were clinical cure or improvement and all-cause mortality.

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 studies were assessed for validity using a scale adapted from Heintjes et al (see Other publications of related interest). Each study was assigned a score for quality based on 10 criteria. Two authors independently assessed the validity of the studies. Any discrepancies were resolved by consensus.

Data extraction
Results for dichotomous outcomes were extracted in order to calculate risk ratios (RR) with 95% confidence intervals (CIs) for intention-to-treat (ITT) or modified intention-to-treat data. Authors or study sponsors were contacted for additional data where required.

Two authors independently extracted the data. Discrepancies were resolved by consensus.

Methods of synthesis
RRs were pooled in a meta-analysis. Weightings and summary estimates for each outcome were based on DerSimonian and Laird random-effects model. The Mantel-Haenszel test was used to test for heterogeneity (defined at p-value <0.2). The extent of any inconsistency was measured using the I² statistic.

For the primary analysis, the included trials compared patients who received an antibacterial with activity against atypical organisms with those who received an antibacterial without activity against atypical organisms. For the secondary analysis, studies that compared different antibacterial drug classes were grouped, provided that both
comparators had similar coverage for atypical organisms.

**Results of the review**

Thirteen studies were included (n=4,314 of whom 3,402 could be analysed). The median quality score was 6.67 (range 6 to 8.17).

There were no significant differences observed between treatments, and no significant heterogeneity was observed between the studies for atypical coverage versus no atypical coverage (six studies).

There was no evidence to suggest that antibacterials active against atypical pathogens were superior to other antibacterials when comparing antibacterials such as fluoroquinolones and macrolides (five studies) or cephalosporins compared with β-lactam/β-lactamase inhibitors (two studies).

Five studies reported 24 deaths (mortality 0.7 per cent). There was no difference in mortality rates between patients treated with atypical agents compared with other drugs and no differences between those treated with fluoroquinolones and macrolides.

**Authors' conclusions**

There was no evidence supporting the superiority of antibacterials active against atypical organisms, or for differences in outcome between drug classes with similar atypical coverage.

**CRD commentary**

The review addressed a clear question with appropriately detailed inclusion criteria. A number of relevant sources appeared to have been considered to identify relevant studies. The literature search was restricted to publications in English and there was no apparent search for unpublished studies, therefore, both publication and language biases may have been present. It was unclear how the studies were selected for inclusion within the review, but appropriate methods were taken to control for error and bias during data extraction and an assessment of the methodological quality of the included studies was undertaken. The methods used for synthesising the studies were appropriate and heterogeneity was explored. The authors’ conclusions reflected the evidence presented, but given some of the uncertainties identified in the review process, the extent to which they were reliable is unclear.

**Implications of the review for practice and research**

Practice: The authors stated that the selection of antibacterials should be based upon side-effect profile, price, physician and patient preferences and resistance-induction considerations.

Research: The authors did not state any implications for research.

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**Other publications of related interest**

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.