Treatment of community-acquired pneumonia with moxifloxacin: a meta-analysis of randomized controlled trials

CRD summary
The authors concluded that moxifloxacin was as safe and effective as other antibiotics for treating community-acquired pneumonia; moxifloxacin showed favourable pathogen eradication rates compared with beta-lactam-based therapy. The authors' conclusions and recommendations for practice do not reflect uncertainties in the evidence and cannot be considered reliable.

Authors' objectives
To compare the efficacy and safety of moxifloxacin versus other antimicrobial agents in the treatment of adults with community-acquired pneumonia.

Searching
PubMed, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), and Web of Science were searched up to December 2011; search terms were reported. Reference lists of retrieved articles and relevant reviews were manually searched, and experts in the field were contacted.

Study selection
Randomised controlled trials (RCTs) that compared the efficacy and safety of moxifloxacin monotherapy versus other antimicrobial agents in the treatment of adults with mild-to-moderate or severe community-acquired pneumonia (as defined in the review) were eligible for inclusion. The primary outcome was treatment success at follow-up (as defined in the review). Secondary outcomes included bacteriological response, probable or possible drug-related adverse events, and all-cause mortality.

Included trials were published from 1999 to 2008; nine trial were multi-centred. Trials compared oral or intravenous moxifloxacin (most administered 400mg/daily) versus various doses and regimens of beta-lactam-based therapies, levofloxacin, or macrolides. The duration of trials ranged from seven to 14 days. Some trials were in outpatients and some in hospitalised patients.

Three reviewers independently screened studies for inclusion.

Assessment of study quality
Two reviewers independently assessed trial quality using the Jadad scoring system; the maximum score was 5 points. Trials that scored more than 4 points were considered high quality, while trials that scored 2 or fewer points were considered low quality.

Data extraction
Three reviewers independently extracted data on a per protocol and intention-to-treat basis to calculate odds ratios and their 95% confidence intervals. Primary authors were contacted for additional information where necessary. Disagreements between reviewers were resolved through consensus or referral to a third reviewer.

Methods of synthesis
A fixed effect model (or random effects model where there was evidence of statistically significant heterogeneity) was used to pool odds ratios and 95% confidence intervals. Statistical heterogeneity was assessed using the $X^2$ and $I^2$ ($I^2 > 50\%$ indicated notable heterogeneity).

Subgroup analyses were performed to assess different types of control and treatment success in patients with severe community-acquired pneumonia. Sensitivity analysis was performed to include only blinded RCTs.

Publication bias was assessed using funnel plots and Egger's test.
Results of the review
Fourteen RCTs (approximately 6,926 patients; ITT 5,793) were included in the review. The authors considered all trials to be high quality with scores ranging from 3 to 5 points.

There were no statistically significant differences between moxifloxacin and other antimicrobial agents in the treatment of community-acquired pneumonia for treatment success (14 RCTs). Subgroup analyses did not significantly alter the findings. There was no evidence of significant statistical heterogeneity for any analyses.

The eradication or presumed eradication of bacteria was higher in the moxifloxacin group compared with comparators (OR 1.47, 95% CI 1.04 to 2.08; 12 RCTs). When subgroup analyses were performed by control type, only moxifloxacin compared with beta-lactam-based therapies showed a statistically significant difference (OR 1.67, 95% CI 1.04 to 2.68; seven RCTs).

There were no statistically significant differences in total adverse events or mortality between moxifloxacin and comparators. Other results were reported in the review.

Authors’ conclusions
Moxifloxacin was associated with similar overall rates of clinical treatment success, mortality, and adverse events when compared with macrolides, beta-lactam-based therapy, and levofloxacin in patients with community-acquired pneumonia. However, moxifloxacin appeared to have superior microbiological eradication efficacy compared to beta-lactam-based therapy.

CRD commentary
The review question and inclusion criteria were clearly defined. The literature search was adequate, but it was unclear whether attempts were made to locate unpublished data. Although formal assessment of publication bias did not indicate any evidence of bias, the limited number of studies and their inconsistency hampered interpretation of the funnel plots. Each stage of the review was performed in duplicate, which reduced the potential for reviewer error and bias.

Appropriate methods were used to pool data. Trial quality was assessed using relevant criteria. The authors considered the RCTs to be of high quality; however, using the authors’ scoring system, the five trials that were not blinded would have been considered of moderate quality, so it would appear that only one trial was of high quality. The authors acknowledged that some trials did not included detailed adverse events, which may have influenced the safety results.

The authors’ conclusions and recommendations for practice did not adequately reflect the imprecision in the results, small effects, inconsistency in effect direction, small sample sizes and low events rates. So, the authors' conclusions do not appear reliable given the uncertainties inherent in the evidence base.

Implications of the review for practice and research
Practice: The authors stated that the once daily dosing of moxifloxacin may be a useful alternative to combination and/or multi-dose antibiotic regimens.

Research: The authors stated that more well-designed, RCTs were needed to confirm the higher pathogen eradication rate of moxifloxacin compared to other antibiotics.

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