Quinolones for treatment of nosocomial pneumonia: a meta-analysis
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CRD summary
This review compared quinolones with other treatments for nosocomial (hospital-acquired) pneumonia. The authors concluded that quinolones may be as effective as comparator antibiotics in terms of clinical cure and mortality, but more effective in achieving microbiological eradication and preventing the development of resistance. This was a well-conducted review and the authors' conclusions are likely to be reliable.

Authors' objectives
To assess the efficacy of quinolones in the treatment of nosocomial pneumonia (NP).

Searching
MEDLINE (from 1975) and EMBASE (from 1988) were searched up to June 2003; some search terms were given. In addition, the references of relevant articles were checked and colleagues were contacted. No language restrictions were applied.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) with 30 or more patients were included in the review. Studies in which less than 40% of the patients were microbiologically evaluable, or in which more than 20% of the patients were lost to follow-up, were excluded from the review.

Specific interventions included in the review
Studies using quinolones that were commercially available at the time of the review were eligible for inclusion. The trials included in the review employed ciprofloxacin (300 to 400 mg) administered every 8 hours or levofloxacin (750 mg) administered daily. The comparators were imipenem-cilastatin and ceftazadime. Some included studies allowed the use of multiple antibiotics.

Participants included in the review
Studies of patients with NP were included in the review if they provided a precise definition of the criteria used to diagnose NP.

Outcomes assessed in the review
The primary outcome was clinical cure, as defined by the trial authors. Death occurring during the trial period was a secondary outcome. Microbiological eradication and the emergence of resistance to therapy were also considered in the review. Microbiological isolates differed considerably amongst the included studies.

How were decisions on the relevance of primary studies made?
Two reviewers assessed the studies for inclusion in the review. Any disagreements were resolved by consensus.

Assessment of study quality
The validity of the studies was assessed using the Jadad scale, which uses the criteria of randomisation, blinding, allocation concealment, and documentation of withdrawals and drop-outs. Two reviewers assessed the studies for validity. Agreement between the reviewers was assessed using the kappa statistic.

Data extraction
Two reviewers extracted the data and any disagreements were resolved by consensus. Primary and secondary outcomes
and microbiological eradication rates were extracted. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated for each outcome.

**Methods of synthesis**

How were the studies combined?
The ORs for each outcome were pooled in a fixed-effect meta-analysis, with an accompanying narrative synthesis. The potential for publication bias was assessed using Begg’s test.

How were differences between studies investigated?
Differences between the studies in terms of study quality, intervention, comparator and cointerventions employed, and microbiological characteristics of the patients, were discussed in the narrative. Statistical heterogeneity was also assessed using the Wolfe statistic.

**Results of the review**

Five RCTs (n=1,186) were included in the review.

In terms of study quality, the median score on the Jadad scale was 6 (range: 5 to 7). A Begg’s funnel plot analysis showed no evidence of publication bias in the review. The authors stated that the Wolfe statistic revealed no statistical heterogeneity between the trials.

Clinical cure (5 RCTs, n=1,186): there was no statistically significant difference between quinolone and the comparator groups; the pooled OR was 1.12 (95% CI: 0.80, 1.55) in favour of quinolones.

Mortality (5 RCTs, n=1,186): there was no statistically significant difference between quinolone and the comparator groups; the pooled OR was 0.87 (95% CI: 0.57, 1.37) in favour of quinolones.

Microbiologic eradication (5 RCTs, n=1,186): the difference between quinolone and the comparator groups approached a level of statistical significance in favour of quinolones; the pooled OR was 1.41 (95% CI: 1.00, 2.00).

Emergence of resistance (3 RCTs, n=899): of the 3 trials that assessed the emergence of resistance, only the results of one were reported. This trial found that the emergence of resistance occurred less often with quinolones than with imipenem-cilistatin: 33% of Pseudomonas aeruginosa isolates with quinolones versus 53% with control.

**Authors’ conclusions**

Quinolones were acceptable options for treating NP, and may be preferable to alternative treatments on the grounds of their cost, convenience and potential for the emergence of resistant bacterial strains. The authors noted that the dosing regimen for ciprofloxacin evaluated in the included trials differed from the approach commonly employed in practice.

**CRD commentary**

The review question and the inclusion criteria were clear. The authors searched two relevant databases and made attempts to identify trials from other sources. The fact that they used no language restrictions in their search and also included an analysis of publication bias, which showed no indication of an effect, makes it less likely that the review was affected by the over-representation of positive trials due to language or publication bias. The authors used appropriate measures to minimise bias and error in the study selection, quality assessment and data extraction processes. They employed an appropriate method of validity assessment (although the results reported were higher than the normal upper-limit for the scale used), and also had a quality indicator among their inclusion criteria. The decision to employ meta-analyses to synthesise the studies was appropriate, particularly as a thorough discussion of both clinical and statistical heterogeneity was also provided. The authors’ conclusions accurately reflect the results of the review and are likely to be reliable. However, the authors pointed out that all but one of the RCTs were completed before 1999, and thus were conducted before recent trends towards increasing infections with meticillin-resistant Staphylococcus aureus.
Implications of the review for practice and research
The authors did not state any implications for practice or further research.

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