Fluoroquinolones compared with beta-lactam antibiotics for the treatment of acute bacterial sinusitis: a meta-analysis of randomized controlled trials

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CRD summary
This review found fluoroquinolones to be comparable to β-lactam antibiotics for acute bacterial sinusitis. However, a tendency towards more adverse events in the fluoroquinolone patients was observed in the sensitivity analyses. Respiratory fluoroquinolones are not recommended for use as a first-line intervention, but may be appropriate in cases where β-lactam antibiotic treatment has failed. Despite the poor reporting of the methodology, the conclusions are probably reliable.

Authors’ objectives
To review the effectiveness and safety of fluoroquinolones in comparison with β-lactam antibiotics for acute bacterial sinusitis.

Searching
MEDLINE (July 1965 to March 2007) and, subsequently, Scopus and the Cochrane CENTRAL Register were searched; the search terms were reported. The bibliographies of retrieved articles were handsearched for relevant studies. Publications in English, French, German, Italian and Greek were eligible.

Study selection
Only randomised controlled trials were eligible for this review; the included studies comprised open-label, double-blind and investigator-blinded designs. The inclusion criteria specified that the eligible intervention was respiratory or non-respiratory fluoroquinolones, and the comparator β-lactam antibiotics. The included studies compared a variety of these drugs against one another. The patients were not restricted by age or gender (mean age 41.1 years; 62.6% female), but they had to have a diagnosis of acute bacterial sinusitis based on clinical criteria (detailed clinical definition provided in the paper). The outcomes were not pre-specified in this review, but included studies reported cure according to clinical criteria, change in symptoms and bacteriological success of treatment.

Two reviewers independently evaluated studies for inclusion.

Assessment of study quality
The included studies were assessed for validity on the basis of the following criteria: randomisation, allocation concealment, masking of the intervention, and the reporting of withdrawals, crossovers between study arms and violations of inclusion criteria.

The authors did not state how the validity assessment was carried out.

Data extraction
Data were extracted from the included studies as 'clinical success' odds ratios (ORs) and 95% confidence intervals (CIs), which combined clinical cure and a substantial improvement in symptoms in the intention-to-treat populations. Safety data were extracted as the total number of adverse events in patients who were assessed for these outcomes. Secondary outcome data were extracted as 'clinical success' in the clinically evaluable population and the bacteriologically evaluable populations.

Two reviewers extracted the data, with any differences being resolved by discussion among all authors.

Methods of synthesis
The authors used a Mantel-Haenszel fixed-effect model for meta-analysis and assessed heterogeneity with the $\chi^2$ and $I^2$
statistics. Where substantial heterogeneity was noted, a DerSimonian and Laird random-effects model was used. Subset analyses were carried out to compare fluoroquinolones with amoxicillin-clavulanate in the clinically evaluable population, and additional analyses assessed respiratory fluoroquinolones and all fluoroquinolones. Sensitivity analyses were used to assess key outcomes in double-blind or investigator-blinded studies. Publication bias was assessed using the funnel plot and Egger's test.

Results of the review
Eleven trials were included in this review: 5 open-label studies (n=3,140), 5 double-blind studies (n=2,194) and an investigator-blinded study (n=445).

Of the 11 trials, the following quality criteria were reported: adequate randomisation (6 trials), allocation concealment (3 trials), masking of the intervention (5 trials), information on withdrawals (7 trials), crossovers of patients (1 trial) and violation of the inclusion criteria (4 trials).

Clinical success in the intention-to-treat population was reported by 5 studies (n=2,133), all comparing respiratory fluoroquinolones and β-lactam antibiotics. No statistically significant benefit was found (OR 1.09, 95% CI: 0.85, 1.39).

Eleven studies (n=4,640) reported on clinical successes in clinically evaluable patients, and showed a benefit in favour of any fluoroquinolone treatment over β-lactam antibiotics for acute bacterial sinusitis (OR 1.24, 95% CI: 1.03, 1.49). A similar result was found when looking at respiratory fluoroquinolones only. The sensitivity analyses reported similar results when restricting the analysis to double-blind or investigator-blinded studies.

Bacteriologic success was evaluated in 5 trials (n=868). The results found that eradication of pathogens was more likely if patients received any fluoroquinolones rather than a β-lactam antibiotic (OR 1.99, 95% CI: 1.24, 3.19).

Four trials (n=1,599) assessed relapse of signs and symptoms of sinusitis in patients who received a respiratory fluoroquinolone versus β-lactam antibiotics. No significant differences were found (OR 0.79, 95% CI: 0.47, 1.33).

Conflicting results were reported for adverse events rates: a meta-analysis of all trials reporting this outcome (9 trials, n=5,018) suggested that there was no significant difference between fluoroquinolones and β-lactam antibiotic groups, whereas a sensitivity analysis of blinded randomised trials (4 trials, n=1,905) found significantly higher rates of adverse events in the fluoroquinolone-treated patients (OR 1.33, 95% CI: 1.09, 1.63).

Authors' conclusions
Respiratory fluoroquinolones were comparable to β-lactam antibiotics for acute bacterial sinusitis. However, a tendency towards more adverse events in the fluoroquinolone patients was observed in the sensitivity analyses. Respiratory fluoroquinolones are not recommended for use as a first-line intervention, but may be appropriate in cases where β-lactam antibiotic treatment has failed.

CRD commentary
This review addressed a clear question. However, the inclusion criteria could have been specified in more detail, particularly in relation to the outcomes. The authors searched some relevant databases but did not report searching for unpublished studies; this might have increased the risk of publication bias. The range of languages covered was likely to have minimised language bias. All of the included studies were assessed for validity, and this was incorporated into some of the sensitivity analyses. A mixture of fixed-effect and random-effects models were used for the meta-analyses, based on tests for heterogeneity, although this may not have been helpful. Tests for publication bias were mentioned but the results were not reported. Despite the incomplete reporting of the methodology, the conclusions are probably reliable.

Implications of the review for practice and research
Practice: The authors stated that respiratory fluoroquinolones are not recommended for use as a first-line intervention for the treatment of acute bacterial sinusitis, but they may be appropriate in cases where β-lactam antibiotic treatment has failed.

Research: The authors did not state any implications for further research.
Funding
Not stated.

Bibliographic details

PubMedID
18362380

DOI

Original Paper URL
http://www.cmaj.ca/

Indexing Status
Subject indexing assigned by NLM

MeSH
Acute Disease; Anti-Bacterial Agents /therapeutic use; Aza Compounds /therapeutic use; Fluoroquinolones /therapeutic use; Humans; Pneumococcal Infections /drug therapy; Quinolines /therapeutic use; Randomized Controlled Trials as Topic; Sinusitis /drug therapy /microbiology; beta-Lactams /therapeutic use

AccessionNumber
12008008130

Date bibliographic record published
09/08/2008

Date abstract record published
01/12/2008

Record Status
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.