Prophylaxis with fluoroquinolones for bacterial infections in neutropenic patients: a meta-analysis

Cruciani M, Rampazzo R, Malena M, Lazzarini L, Todeschini G, Messori A, Concia E

Authors' objectives
To assess the efficacy of fluoroquinolones, with or without prophylaxis, for gram-positive bacteraemia in neutropenic patients with cancer.

Searching
MEDLINE was searched from January 1984 to October 1994 using the keywords 'neutropenia/agranulocytosis' and 'bacterial infections'. Additional literature was obtained by examining Current Contents and the bibliographies of retrieved articles.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were included.

Specific interventions included in the review
Fluoroquinolones versus control (trimethoprim-sulfamethoxazole, oral nonabsorbable antibiotics or placebo), and fluoroquinolones plus antimicrobial agents active against gram-positive microorganisms (penicillin G or V, vancomycin or a macrolide) with control regimens (fluoroquinolones alone, or oral nonabsorbable antibiotics).

Participants included in the review
Granulocytopenic patients undergoing chemotherapy for cancer were included.

Outcomes assessed in the review
Bacteraemia, fever and infection-related mortality were assessed.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection. To be included, studies had to be randomised and comparing a control regimen with fluoroquinolones alone, or in combination with gram-positive prophylaxis for prevention of bacterial infections in granulocytopenic patients receiving chemotherapy for cancer. Efficacy had to be assessed in terms of infection-related morbidity and mortality.

Assessment of study quality
Two previously developed quality assessment instruments were modified for use in this review. The 15-category instrument evaluates quality in study design (inclusion, exclusion criteria, number of patients excluded and reasons, definition of drug and control regimens, blinding, prognostic factors between groups, definition of outcome measure) and data analysis and presentation of results (documentation of dates of study, patient withdrawals, raw data, study power, recording of p-values for major outcomes, and confidence intervals). Four reviewers blinded to study titles, journals, authors and institutions independently evaluated the quality of each article using the quality assessment instrument. Values of 0 to 1.0 were assigned for each item (range: 0 - 15). Any disagreements were resolved by consensus.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.
**Methods of synthesis**

How were the studies combined?
The studies were combined by meta-analysis using both the Mantel-Haenszel fixed-effect model and the DerSimonian and Laird random-effects model.

How were differences between studies investigated?
Equations reported in Collins et al. (see Other Publications of Related Interest) were used to determine heterogeneity. Meta-analyses were performed separately for patients receiving fluoroquinolones alone or fluoroquinolones plus gram-positive prophylaxis. Subgroup analyses were carried out where heterogeneity was found.

**Results of the review**

Nineteen RCTs with a total of 2,112 patients: 13 studies with a total of 1,155 patients for fluoroquinolones versus control, and 6 studies with 957 patients for fluoroquinolones plus antimicrobial agents versus control.

Prophylaxis with fluoroquinolones was shown to significantly reduce the frequency of gram-negative bacteraemia (odds ratio, OR 0.09, 95% confidence interval, CI: 0.05, 0.16, p<0.001), without affecting the frequency of gram-positive bacteraemia (OR 1.05, CI: 0.76, 1.45, p=0.7) or infection-related mortality (OR 0.79, CI: 0.47, 1.34, p=0.4). The addition of gram-positive prophylaxis to fluoroquinolone prophylaxis significantly reduced the frequency of gram-positive bacteraemia (OR: 0.46, CI: 0.33, 0.63, p<0.001), without affecting the incidence of fever-related morbidity (OR 0.83, CI: 0.62, 1.13, p=0.2) or infection-related mortality (OR 0.74, CI: 0.40, 1.38, p=0.3). Significant heterogeneity was found for the outcomes of gram-positive bacteraemia and fever in the first analysis, and for gram-positive bacteraemia in the second. Subgroup analyses were performed.

**Authors’ conclusions**
The results of our meta-analyses suggest that prophylaxis with fluoroquinolones for bacterial infections in granulocytopenic patients reduces the incidence of gram-negative bacteraemia among these patients, without increasing the incidence of gram-positive bacteraemia. This benefit was not observed for patients who received control regimens. Moreover, the addition of gram-positive coverage to fluoroquinolone prophylaxis effectively reduced the overall incidence of gram-positive bacteraemia, especially that due to streptococcal species.

**CRD commentary**
This appears to be a well-conducted systematic review, with detailed reporting of the methods used. The authors note that the quality assessment of individual studies was for descriptive purposes only. There was evidence of heterogeneity among studies in some of the outcomes measured; this remained in subgroup analyses for the first analysis but disappeared in the second analysis.

**Bibliographic details**

**PubMedID**
8909847

**Other publications of related interest**
MeSH
Anti-Bacterial Agents /therapeutic use; Anti-Infective Agents /therapeutic use; Bacteremia /drug therapy /prevention & control; Drug Therapy, Combination; Fluoroquinolones; Gram-Negative Bacterial Infections /drug therapy; Gram-Positive Bacterial Infections /drug therapy /prevention & control; Humans; Macrolides; Neoplasms /complications /microbiology; Neutropenia /microbiology; Penicillins /therapeutic use; Vancomycin /therapeutic use

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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.