Effectiveness and safety of once-daily aminoglycosides: a meta-analysis
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Authors' objectives
To evaluate the effectiveness and safety of once-daily versus several-times-daily aminoglycosides.

Searching
MEDLINE was searched from January 1988 to October 1995 using the terms 'aminoglycoside', 'netilmicin', 'amikacin', 'gentamicin', 'tobramycin', 'once-daily' and 'single daily dosing'. Additional literature was obtained by examining pertinent review articles and reference lists from retrieved articles. Only English language articles were considered.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) comparing the result of once-daily with several-times-daily aminoglycosides were included.

Specific interventions included in the review
Aminoglycosides: amikacin, netilmicin, or gentamicin (generally used in combination with other antibiotics).

Participants included in the review
Non-neutropenic adult patients with clinical or bacterial symptoms of infection were included.

Outcomes assessed in the review
(1) Clinical effectiveness, defined as the resolution of signs and symptoms of infection. (2) Nephrotoxicity, defined as an elevation in the serum creatinine concentration of at least 0.3 mg/dL. (3) Ototoxicity, defined as a hearing loss of at least 15 dB at any frequency in one or both ears.

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.

Assessment of study quality
A quality score (range: 0 to 100) was assigned to each study, based on the method of Chalmers et al. (see Other Publications of Related Interest) for quality assessment of RCTs. The studies were reviewed independently by two reviewers who were blinded to the source and authors.

Data extraction
The studies were reviewed independently by two reviewers.

Methods of synthesis
How were the studies combined?
The odds ratios from the individual studies were combined using the Mantel-Haenszel fixed-effect model.

How were differences between studies investigated?
The statistical heterogeneity across the studies was tested. Sensitivity analysis and subgroup analysis were conducted according to the type of aminoglycosides, industry financial support, the quality score of studies, and the sound frequency range used in audiometry.
Results of the review
Eighteen studies (a total of 2,317 patients) met the criteria for inclusion.

The testing of the statistical heterogeneity across the studies was not significant. The mean of quality scores was 55 (standard deviation 14, range: 27 to 74). The clinical effectiveness in the once-daily group was higher than that in the control group (pooled odds ratio 1.47, 95% confidence interval, CI: 1.13, 1.94). The overall odds ratios for ototoxicity and nephrotoxicity were 0.56 (95% CI: 0.26, 1.16) and 0.6 (95% CI: 0.4, 0.86), respectively.

Authors' conclusions
Treatment with single daily doses of aminoglycosides seems to be more effective, less nephrotoxic, and as ototoxic as multiple doses daily.

CRD commentary
This was a well-presented meta-analysis. Potential publication bias was not discussed.

Bibliographic details

PubMedID
8734674

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Adult; Aged; Amikacin /administration & dosage /adverse effects; Anti-Bacterial Agents /administration & dosage /adverse effects; Controlled Clinical Trials as Topic; Drug Administration Schedule; Ear Diseases /chemically induced; Gentamicins /administration & dosage /adverse effects; Humans; Infection /drug therapy; Kidney Diseases /chemically induced; Middle Aged; Netilmicin /administration & dosage /adverse effects

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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.