Meta-analysis: A single daily dose of aminoglycosides is as effective as multiple daily dosing with less nephrotoxicity


Objective
To determine the efficacy and toxicity of aminoglycosides when given as a single daily dose compared with multiple daily doses.

Data sources
Studies were identified by searching MEDLARS databases (January 1966 to January 1995) with the keywords aminoglycoside and the names of individual drugs and by scanning the bibliographies of identified articles.

Study selection
Studies were selected if they were randomized controlled trials comparing a single daily dose of an aminoglycoside with the same total daily dose given multiple times each day. Studies were excluded if the aminoglycosides were used for surgical prophylaxis, there were no identifiable outcomes for efficacy and toxicity, or aminoglycosides were included in combinations differing between treatment groups.

Data extraction
Data were extracted on the clinical setting and anatomic sites of infection; number of randomized and evaluable patients; specific aminoglycoside used; route, dose, and dosing frequency; duration of treatment; bacteriologic data; use of concurrent antibiotics; definitions and number of failures of antibiotic treatment; and definitions and number of events of nephrotoxicity and ototoxicity. Clinical response took priority over bacteriologic results. For the main analysis, a 30% increase in serum creatinine level was used to define nephrotoxicity.

Main results
21 trials, involving 3091 patients with bacterial infection, met the selection criteria. Data pooled from 19 trials showed that a single daily dose produced a nonsignificant increase in clinical successes (90% vs 87%, risk ratio 1.03, 95% CI 0.99 to 1.07, P = 0.11). Single-dose compared with multiple-dose regimens reduced nephrotoxicity (overall rate weighted by study size 5.5% vs 7.7%, P = 0.05). This absolute risk reduction of 2.2% means that 56 patients (weighted calculation) would need to be treated with a single daily dose (rather than multiple doses) to prevent 1 additional nephrotoxic event; CI 29 to 626; the relative risk reduction was 26%, CI 0% to 46%).* Ototoxicity did not differ between the 2 dosing regimens, but the statistical power to detect a difference with the pooled results was low. There was also no difference in mortality. The same findings applied to trials with high rates of Pseudomonas infections and to trials in febrile neutropenic patients.

Conclusion
A single daily dose of aminoglycosides in patients without pre-existing renal impairment is as effective as multiple daily dosing, has a lower risk for nephrotoxicity, and has no greater risk for ototoxicity or death.

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*Numbers calculated from data in article.

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