

primary studies - published RCT

## Once-daily tobramycin in cystic fibrosis: better for clinical outcome than thrice-daily tobramycin but more resistance development?.

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**Author:** Burkhardt O

### Study design (if review, criteria of inclusion for studies)

single-centre, open, randomized, controlled, non-blinded study

### Participants

33 adult CF patients (20 females, 19-37 years)

### Interventions

intravenous tobramycin (10 mg/kg/day) for 14 days given either as single dose once a day (Q24; 17 patients) or divided into three equal doses every 8 h (Q8; 16 patients).

### Outcome measures

Tobramycin serum concentrations and MICs for *Pseudomonas aeruginosa* were determined on days 1 and 14. The clinical outcome parameter, correlated to PK/PD indices, was the percentage predicted forced expiratory volume in 1 s (FEV(1)% pred.).

### Main results

FEV(1)% pred. improved significantly for both treatments. There was a log-linear relationship between C(max)/MIC and FEV(1)% pred. and AUC/MIC and FEV(1)% pred. for both treatments. For equal values of AUC24/MIC, however, Q24 treatment provided better improvement in lung function than Q8 dosing, whereas C(max)/MIC did not show any dosing interval dependence. A statistically significant increase was observed for MIC (day 1) versus MIC (day 14) for Q24 treatment, however, no such difference was observed for Q8 treatment.

### Authors' conclusions

The most important PK/PD parameter for clinical outcome in CF patients was C(max)/MIC. Outcome prediction of AUC(24)/MIC was dependent on the regimen. The increase of *P. aeruginosa* resistance after once-daily administration is linked to a long dosing interval. More and larger studies are needed to optimize the dosing regimen for maximum clinical outcome with minimum resistance development.

<http://dx.doi.org/10.1093/jac/dkl328>

### See also

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### Keywords

Adult; Anti-Bacterial Agents; Bacterial Infections; Infection; pharmacological\_intervention; *Pseudomonas aeruginosa*; *Pseudomonas*; resistance; Respiratory Tract Diseases; Respiratory Tract Infections; Tobramycin; Intravenous; Aminoglycosides;