

primary studies - published RCT

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

Code: PM16885180

Year: 2006 **Date:** 2006

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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

J Antimicrob Chemother. 2006 Oct;58(4):822-9. Epub 2006 Aug 2.

Keywords

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