primary studies - published RCT

Once versus three-times daily regimens of tobramycin treatment for pulmonary exacerbations of cystic fibrosis--the TOPIC study: a randomised controlled trial.

Code: PM15708100 **Year:** 2005 **Date:** 2005 **Author:** Smyth A

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

Parallel design.

Participants

Once daily n = 107 (63 males); age range 5.1 to 50.4 years. Per protocol analysis (n = 219). Thrice daily n = 112 (68 males); age range 5.5 to 43.3 years. Pulmonary exacerbation defined. 21 centres in the UK. Central randomisation, stratified by centre and adult versus paediatric.

Interventions

14 days of treatment. Once-daily dosing (10 mg/kg/day) versus thrice-daily dosing (10 mg/kg/day) of tobramycin or dose last shown to give therapeutic levels. Combination therapy with ceftazidime.

Outcome measures

Weight (kg). Lung function: FEV1 and FVC. Ototoxicity. Nephrotoxicity: serum creatinine & urine NAG.

Main results

219 patients (107 once daily, 112 three-times daily) completed the study per protocol. None was lost to follow-up, although 20 discontinued intervention. Of 122 patients assigned to once daily treatment, three did not receive the study regimen. The mean change in FEV1 (% predicted) over 14 days was similar on the two regimens (10.4% [once daily] vs 10.0% [three-times daily]; adjusted mean difference 0.4% [95% CI -3.3 to 4.1]). Mean% change in FEV1 from baseline was also similar in both treatments (21.9% vs 22.1%; -0.1% [-8.0 to 7.9]). There was no significant difference in% change in creatinine from baseline (-1.5% [once daily] vs 1.7% [three-times daily]). However, in children, once daily treatment was significantly less nephrotoxic than was thrice daily (mean% change in creatine -4.5% [once daily] vs 3.7% [thrice daily]; adjusted mean difference -8.0%, 95% CI -15.7 to -0.4). No patients developed hearing loss during the study, although two reported acute dizziness and were withdrawn from the study.

Authors' conclusions

Intravenous tobramycin has equal efficacy if given once or three-times daily (with ceftazidime) for pulmonary exacerbations of cystic fibrosis. The once daily regimen might be less nephrotoxic in children.

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See also

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Keywords

Adolescent; Adult; Anti-Bacterial Agents; Bacterial Infections; Ceftazidime; Child; Combined Modality Therapy; Drug Administration Schedule; Infection; Intravenous; pharmacological_intervention; Pseudomonas aeruginosa; Pseudomonas; Respiratory Tract Diseases; Respiratory Tract Infections; Tobramycin; Exacerbation; Cephalosporins; Aminoglycosides;