primary studies - published RCT

Intravenous or oral antibiotic treatment in adults and children with cystic fibrosis and Pseudomonas aeruginosa infection: the TORPEDO-CF RCT.

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

Phase IV, multicentre, parallel-group, randomised controlled trial.

Participants

Individuals with cystic fibrosis aged >â€‰28 days old who had never had a P. aeruginosa infection or who had been infection free for 1 year.

Interventions

Fourteen days of intravenous ceftazidime and tobramycin or 3 months of oral ciprofloxacin. Inhaled colistimethate sodium was included in both regimens over 3 months. Consenting patients were randomly allocated to either treatment arm in a 1â€‰:â€‰1 ratio using simple block randomisation with random variable block length.

Outcome measures

The primary outcome was eradication of P. aeruginosa at 3 months and remaining free of infection to 15 months. Secondary outcomes included time to reoccurrence, spirometry, anthropometrics, pulmonary exacerbations and hospitalisations. Primary analysis used intention to treat (powered for superiority). Safety analysis included patients who had received at least one dose of any of the study drugs. Cost-effectiveness analysis explored the cost per successful eradication and the cost per quality-adjusted life-year.

Main results

Between 5 October 2010 and 27 January 2017, 286 patients were randomised: 137 patients to intravenous antibiotics and 149 patients to oral antibiotics. The numbers of participants achieving the primary outcome were 55 out of 125 (44%) in the intravenous group and 68 out of 130 (52%) in the oral group. Participants randomised to the intravenous group were less likely to achieve the primary outcome; although the difference between groups was not statistically significant, the clinically important difference that the trial aimed to detect was not contained within the confidence interval (relative risk 0.84, 95% confidence interval 0.65 to 1.09; pâ€‰=â€‰0.184). Significantly fewer patients in the intravenous group (40/129, 31%) than in the oral group (61/136, 44.9%) were hospitalised in the 12 months following eradication treatment (relative risk 0.69, 95% confidence interval 0.5 to 0.95; pâ€‰=â€‰0.02). There were no clinically important differences in other secondary outcomes. There were 32 serious adverse events in 24 participants [intravenous: 10/126 (7.9%); oral: 14/146 (9.6%)]. Oral therapy led to reductions in costs compared with intravenous therapy (-Â£5938.50, 95% confidence interval -Â£7190.30 to -Â£4686.70). Intravenous therapy usually necessitated hospital admission, which accounted for a large part of this cost. LIMITATIONS: Only 15 out of the 286 participants recruited were adults - partly because of the smaller number of adult centres participating in the trial. The possibility that the trial participants may be different from the rest of the cystic fibrosis population and may have had a better clinical status, and so be more likely to agree to the uncertainty of trial participation, cannot be ruled out.

Authors' conclusions

Intravenous antibiotics did not achieve sustained eradication of P. aeruginosa in a greater proportion of cystic fibrosis patients. Although there were fewer hospitalisations in the intravenous group during follow-up, this confers no advantage over the oral therapy group, as intravenous eradication frequently requires hospitalisation. These results do not support the use of intravenous antibiotics to eradicate P. aeruginosa in cystic fibrosis.

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See also

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Keywords

Anti-Bacterial Agents; Bacterial Infections; Infection; Inhalation OR nebulised; Intranasal; nebuliser; pharmacological_intervention; Pseudomonas aeruginosa; Pseudomonas; Respiratory Tract Diseases; Respiratory Tract Infections; Ceftazidime; Tobramycin; Exacerbation; Aminoglycosides; Monobactams; Cephalosporins; Quinolones; other anti-bacterial agents; oral; Ciprofloxacin; colistimethate;