

A comparative study of hypertonic saline, daily and alternate-day rhDNase in children with cystic fibrosis

R Suri^{1,2}

C Wallis^{1*}

A Bush²

S Thompson³

C Normand⁴

M Flather⁵

R Grieve⁶

C Metcalfe³

B Lees⁵

¹ Respiratory Unit, Great Ormond Street Hospital for Children NHS Trust, London, UK

² Department of Respiratory Paediatrics, Royal Brompton and Harefield NHS Trust, London, UK

³ Medical Research Council Biostatistics Unit, Institute of Public Health, Cambridge, UK

⁴ Department of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, UK

⁵ Clinical Trials and Evaluation Unit, Royal Brompton and Harefield NHS Trust, London, UK

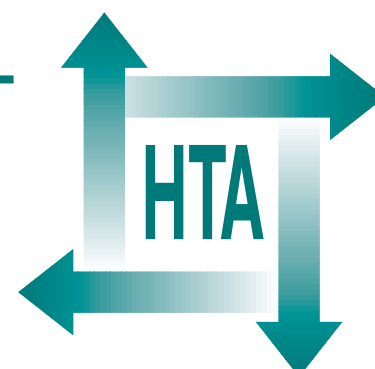
⁶ Department of Public Health and Policy, London School of Hygiene and Tropical Medicine, UK

* Corresponding author

Executive summary

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Executive summary

Objectives

The objective of this study was to compare the efficacy and cost-effectiveness of daily recombinant human deoxyribonuclease (rhDNase), alternate-day rhDNase and hypertonic saline (HS) in the treatment of children with cystic fibrosis (CF).

Design

This was an open-label, active treatment randomised crossover trial.

Setting and participants

Children with a confirmed diagnosis of CF were recruited from two large CF centres in London, the Great Ormond Street Hospital for Children NHS Trust and the Royal Brompton and Harefield NHS Trust. Two inclusion criteria were age between 5 to 18 years and capacity to perform spirometry. The third inclusion criterion was the requirement to either be currently using rhDNase or to have a forced expiratory volume in 1 second (FEV₁) of less than 70% of the predicted value, which is a generally accepted level for the clinical introduction of rhDNase therapy. Exclusion criteria were inability to attend appointments or take the study medication, known severe hypersensitivity to rhDNase or HS, isolation of *Burkholderia cepacia* in the sputum, receiving research medication as part of another trial within the past 4 weeks and being pregnant or breastfeeding. To ensure that patients were enrolled when they were clinically stable, they had to be free of any lower respiratory tract infection requiring a change in antibiotics, steroids or bronchodilator treatment, during the 14 days before randomisation.

Interventions

Each patient was allocated consecutively to 12 weeks of treatment with once-daily 2.5 mg rhDNase, alternate-day 2.5 mg rhDNase or twice-

daily 5 ml of 7% HS, in random order. There was a 2-week washout period between treatments.

Main outcome measures

Patients were assessed at the beginning and end of each of the three treatment periods. The primary outcome measure was FEV₁. Secondary outcome measures were forced vital capacity, number of pulmonary exacerbations, weight gain, quality of life, exercise tolerance, total healthcare cost and relative cost-effectiveness.

Results

A total of 48 children were recruited to the study. Following 12 weeks of treatment, there was a mean increase in FEV₁ over baseline of 16% (standard deviation (SD) 25%), 14% (SD 22%) and 3% (SD 21%) with daily rhDNase, alternate-day rhDNase and HS, respectively. Comparing daily rhDNase with alternate-day rhDNase, there was no evidence of difference between the treatments (2%; 95% confidence interval (CI), -4% to +9%; $p = 0.55$). However, daily rhDNase showed a significantly greater increase in FEV₁ compared with HS (8%; 95% CI, 2% to 14%; $p = 0.01$). The difference in cost between daily rhDNase and alternate-day rhDNase was £513 (95% CI, -£546 to £1510) and between daily rhDNase and HS it was £1409 (95% CI, £440 to £2318). None of the other secondary outcome measures showed significant differences between the treatments.

Conclusions and research recommendations

Alternate-day rhDNase appears to be as effective as daily rhDNase in CF and, on average, reduces health service costs. It appears that 7% HS is not as effective as daily rhDNase, although there was some variation in individual response.

To support our results, a follow-up long-term parallel trial comparing daily rhDNase with alternate-day rhDNase, which includes a health economic analysis, should be performed.

Publication

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NHS R&D HTA Programme

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Initially, six HTA panels (pharmaceuticals, acute sector, primary and community care, diagnostics and imaging, population screening, methodology) helped to set the research priorities for the HTA Programme. However, during the past few years there have been a number of changes in and around NHS R&D, such as the establishment of the National Institute for Clinical Excellence (NICE) and the creation of three new research programmes: Service Delivery and Organisation (SDO); New and Emerging Applications of Technology (NEAT); and the Methodology Programme.

This has meant that the HTA panels can now focus more explicitly on health technologies ('health technologies' are broadly defined to include all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care) rather than settings of care. Therefore the panel structure has been redefined and replaced by three new panels: Pharmaceuticals; Therapeutic Procedures (including devices and operations); and Diagnostic Technologies and Screening.

The HTA Programme continues to commission both primary and secondary research. The HTA Commissioning Board, supported by the National Coordinating Centre for Health Technology Assessment (NCCHTA), will consider and advise the Programme Director on the best research projects to pursue in order to address the research priorities identified by the three HTA panels.

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The National Coordinating Centre for Health Technology Assessment,
Mailpoint 728, Boldrewood,
University of Southampton,
Southampton, SO16 7PX, UK.
Fax: +44 (0) 23 8059 5639 Email: hta@soton.ac.uk
<http://www.ncchta.org>

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