ORIGINAL RESEARCH LETTER

The role of high-flow nasal therapy in bronchiectasis: a *post hoc* analysis

To the Editor:

High-flow nasal therapy (HFNT) is a gas delivery system that provides heated and humidified air or supplemental oxygen by nasal cannula. The role of HFNT in airways disease has primarily focused on COPD. Studies in patients with COPD have demonstrated improvement in quality-of-life scores and reduced acute exacerbations with HFNT use [1, 2].

Humidification therapy offers a promising management approach for patients with bronchiectasis because HFNT improves mucociliary clearance [3]. Improving airway clearance is vital for breaking the "vicious cycle" of recurrent infections and airway inflammation [4]. Only one previous study, Rea *et al.* [5], has evaluated HFNT in patients with stable bronchiectasis. This was an open-label, randomised, controlled trial in patients with either COPD or bronchiectasis. Overall, it found that HFNT significantly decreased exacerbation days, increased time to exacerbation and reduced exacerbation frequency compared to usual care. Quality-of-life scores also improved significantly with humidification therapy. However, the study did not assess benefit in patients with COPD or bronchiectasis separately.

We therefore decided to undertake a *post hoc* analysis to evaluate the effect of humification therapy on the patients with bronchiectasis in the study by Rea *et al.* [5].

The full study methodology is described in the original manuscript [5]. In brief, the 12-month study recruited patients with either COPD or bronchiectasis, randomising study participants to HFNT *versus* usual care. Specific bronchiectasis diagnosis was confirmed by high-resolution computed tomography. This was an open-label study with no sham treatment involved. The treatment arm provided humidified air, fully saturated at 37°C at a flow rate of 20–25 $L \cdot min^{-1}$, delivered *via* Optiflow nasal cannulae connected to a MR880 humidifier (Fisher and Paykel Healthcare, Auckland, New Zealand). Patients were instructed to use the equipment for 2 or more hours per day in their home with flow rates, either 20 or 25 $L \cdot min^{-1}$, set as per patient tolerance. The New Zealand Health and Disability Ethics Committee approved the study and all participants provided written informed consent.

Statistical analyses comparing HFNT and control were performed in the generalised linear model framework for normal or Poisson data, or with the proportional hazards survival model for time to first exacerbation, allowing inclusion of demographic variables (sex, ethnic group, age), number of respiratory admissions in the previous year, and relevant pre-treatment covariate where available. Results are based on model-adjusted predicted means.

Forty-five (41.7%) of the 108 study participants recruited had a diagnosis of bronchiectasis. Within the bronchiectasis group, 26 of the 45 (58%) were assigned HFNT. The mean±SD age of HFNT patients in the bronchiectasis group was 63±11.4 years and for control patients 65±13.9 years. In the bronchiectasis group 58% of HFNT patients were female, as were 63% of control patients. Regarding smoking, 46% and 63% were ex-smokers in the HFNT and control groups, respectively. Overall withdrawal rates and explanation for withdrawal during the study are documented in the initial study [5].

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High-flow nasal therapy significantly reduces exacerbation rates and improves quality of life in patients with stable bronchiectasis. High-flow nasal therapy is therefore a potential treatment option for patients with bronchiectasis. https://bit.ly/2JFXuQc

Cite this article as: Good WR, Garrett J, Hockey HUP, *et al.* The role of high-flow nasal therapy in bronchiectasis: a *post hoc* analysis. *ERJ Open Res* 2021; 7: 00711-2020 [https://doi.org/10.1183/23120541.00711-2020].

TABLE 1 Bronchiectasis group trial end-points

Exacerbation end-points	HFNT	Control	Rate ratio (95% CI)	p-value
Rate, number per patient per year	2.39	3.48	0.69 (0.49, 0.97)	0.034
Annual exacerbation days (geometric mean)	10.3	29.9	0.32 (0.14, 1.02)	0.056
Days to first exacerbation (predicted median)	84	54	0.70[#] (0.35, 1.40)	0.316
Secondary end-points	**Change from baseline**		**Difference (95% CI)**	**p-value**
	HFNT	**Control**		
FEV_1 L	0.145	0.035	0.11 (−0.037, 0.257)	0.139
FVC L	0.115	−0.104	0.22 (−0.031, 0.468)	0.084
St George's respiratory questionnaire score[¶]				
Total	−12.3	−1.2	−11.0 (−20.7, −1.3)	0.028
Symptoms	−16.9	−9.8	−7.1 (−21.0, 6.8)	0.308
Activity	−6.3	3.3	−9.6 (−20.7, 1.5)	0.087
Impacts	−14.7	−1.6	−13.1 (−23.7, −2.4)	0.018
6-minute walk distance m	−16.2	−33.3	−17.1 (−62.3, 28.1)	0.445

HFNT: high-flow nasal therapy; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity. [#]: hazard ratio; [¶]: scores range from 0 to 100, with low scores indicating improvement; a change of four or more units is deemed clinically meaningful.

In the patients with bronchiectasis, the modelled exacerbation rate was 3.48 per patient per year in the control group and 2.39 in the HFNT group, corresponding to a 31.3% relative reduction with HFNT (rate ratio 0.69, 95% CI 0.49–0.97; p=0.03) (table 1, exacerbation end-points).

At enrolment, baseline mean±SD lung function for the bronchiectasis group demonstrated: HFNT forced expiratory volume in 1 s (FEV_1) of 1.51±0.57 L, HFNT FEV_1 (% of pred.) of 56.5±20.2%; control FEV_1 of 1.05±0.42 L, and control FEV_1 (% of pred.) of 42.42±15.2%. At 12 months, there were greater increases in FEV_1 and forced vital capacity (FVC) in the HFNT group than in the control group, although the results were not statistically significant (table 1, secondary end-points).

The St George's Respiratory Questionnaire (SGRQ) "total" score at baseline in the patients with bronchiectasis was 46.6 units and 50.2 units for HFNT and control groups, respectively, indicating poor health status. At 12 months the "total" and "impacts" components of the SGRQ score improved significantly in favour of the HFNT group compared with the control group (table 1, secondary end-points).

Changes in mean 6-minute walking distance did not differ significantly between the HFNT and control groups for the patients with bronchiectasis.

This *post hoc* analysis provides information on the effect of HFNT in patients with stable bronchiectasis. HFNT significantly reduced exacerbation rates and improved quality of life compared with usual care and is therefore a potential treatment option for patients with bronchiectasis.

The mechanism of action of HFNT is multifactorial. Heating to 37°C and the resulting humidification improve ciliary function and mucus hydration, ensuring optimal mucociliary clearance [3, 6]. In addition, the high flow delivered by HFNT exerts positive airway pressure, which has the associated benefits of improved alveolar recruitment, increased tidal volume, reduced work of breathing and improved dead-space washout [7–9].

Our *post hoc* analysis demonstrated that even with a relatively short duration of HFNT (average 1.7 $h \cdot day^{-1}$), patients with bronchiectasis had improved outcomes. More recent studies focusing on patients with COPD have used a longer duration of HFNT (~6 $h \cdot day^{-1}$) [1, 2]. Given patients with bronchiectasis suffer from impaired mucociliary clearance and ciliary dyskinesia as a result of chronic infection and neutrophilic inflammation [4, 10, 11], it is feasible that HFNT benefited our study patients with bronchiectasis primarily through improved airway clearance. Further research investigating whether a longer duration of HFNT results in additional benefit in patients with bronchiectasis is warranted. Other treatment options include HFNT for defined periods during the day at the time when patients undertake chest clearance activities, or overnight use.

There is a paucity of literature investigating HFNT and patients with stable bronchiectasis. Only the study by Rea *et al.* [5] has included patients with stable bronchiectasis. Similarly, only one study has investigated

HFNT in patients with acute exacerbations of airways disease [12]. This feasibility study enrolled patients with coexisting COPD and bronchiectasis and found that HFNT increased mucus clearance and reduced dyspnoea.

There are several limitations that need to be highlighted. Firstly, this is a *post hoc* analysis and, despite the radiologically confirmed bronchiectasis diagnosis and clear inclusion criteria, this was not the study's primary patient group. Consequently, the study did not characterise the patients with bronchiectasis using severity scores and more detailed airway inflammation markers were not analysed. The sub-study size is small and, even though the results are favourable, further larger, multicentre studies need to be undertaken for confirmation.

Overall, HFNT with humidification is a promising treatment for bronchiectasis and further larger studies are required. This is particularly important given the limited treatment options available for patients with bronchiectasis.

William R. Good[1,2], Jeffrey Garrett[2], Hans U.P. Hockey[3], Lata Jayaram[4,5], Conroy Wong[1,2] and Harold Rea[1,2]

[1]Dept of Medicine, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand. [2]Dept of Respiratory Medicine, Middlemore Hospital, Counties Manukau District Health Board, Otahuhu, New Zealand. [3]Biometrics Matters Ltd, Hamilton, New Zealand. [4]Dept of Respiratory Medicine, Western Health, Melbourne, VIC, Australia. [5]Melbourne Medical School, The University of Melbourne, Melbourne, VIC, Australia.

Correspondence: William R. Good, Counties Manukau District Health Board, Respiratory Medicine, 100 Hospital Road, Middlemore Hospital, Otahuhu, Auckland, New Zealand.
E-mail: William.Good@middlemore.co.nz

Received: 30 Sept 2020 | Accepted after revision: 23 Nov 2020

Support statement: The original study was funded by Fisher and Paykel Healthcare Ltd. Funding information for this article has been deposited with the Crossref Funder Registry.

Conflict of interest: W.R. Good has nothing to disclose. J. Garrett has nothing to disclose. H.U.P. Hockey reports their work for the current study was performed under contract for Fisher & Paykel Healthcare Limited. L. Jayaram has nothing to disclose. C. Wong has nothing to disclose. H. Rea has nothing to disclose.

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