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CASE REPORT

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A novel therapy for intractable chronic cough

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Abstract

Two cases of intractable chronic cough improved significantly with humidified high flow therapy (HHFT). A 59-year-old woman with Primary Sjogren's disease and interstitial lung disease, was trialled on a Fisher and Paykel myAIRVO™ system. She reported sustained benefits of uninterrupted sleep and increased socialization with tapering use of HHFT. A 67-year-old woman with idiopathic pulmonary fibrosis also benefited from the use of myAIRVO™. She had relentless cough with minimal movement, and nocturnal cough causing fragmented sleep. Her cough subsided considerably with continuous HHFT, but recurred without. Both patients reported significant reductions in the cough visual analogue scale. The mechanisms by which HHFT improve intractable cough may include reducing airway dryness, inhibition of neutrophil inflammation and mucus obstruction, and splinting of the airways. HHFT significantly improved cough and health-related quality of life in two patients with interstitial lung disease. Further research is warranted to explore the role of domiciliary HHFT.

KEYWORDS
chronic cough, humidified high flow therapy, intractable cough

INTRODUCTION

Intractable chronic cough (CRC) is a challenging condition to manage. Once contributing conditions such as airway disease, gastroesophageal reflux disease (GORD), postnasal drip, and laryngeal hyperresponsiveness have been addressed, patients are left with limited therapeutic options. This is frustrating given the significant reductions in quality of life associated with chronic cough.[1] We report the use of humidified high flow therapy (HHFT) as a potential novel treatment option for patients with intractable chronic cough.

CASE REPORT

Case one

A 59 year never smoking woman with primary Sjogren's disease was referred with intractable chronic cough despite inhaled corticosteroids, nebulised saline, artificial saliva spray and hydroxychloroquine. She had a dry cough for 9 years which was associated with significant xerostomia, bad dentition, and frequent dry retching. Nocturnal cough was particularly troublesome, resulting in fragmented sleep and consequent excessive daytime sleepiness. The cough was aggravated by exercise, change in weather, and strong odours. Airway disease, post-nasal drip, and gastroesophageal reflux disease were excluded. A bronchoscopy demonstrated severely dry airways with no underlying endobronchial lesion. She had normal ventilatory function: FEV_1 2.77 L (108% predicted), FVC 3.39 L (105% predicted), FER 82%, and gas transfer (DLco) was only mildly reduced 17.7 mL/min/mmHg (79% predicted). A high-resolution computerized tomography (HRCT) chest scan revealed mild interstitial lung disease (ILD). A transthoracic echocardiogram was unremarkable.

The patient was trialled on a MyAIRVO™ system, which delivers humidified high flow air through an Optiflow nasal cannula. Within 20 minutes of commencing HHFT at 15 L/min of air, her cough ceased. Over the course of four years she weaned her use of HHFT from overnight every night plus 2–4 hours during the day, to utilizing the system for the first 3 hours of sleep for two nights a week. She now enjoys uninterrupted sleep throughout the night (even during nights between use of HHFT), with no episodes of nocturnal cough. Additionally, she is coughing less throughout

the day despite no daytime use of HHFT. She reports reduction in her fear of leaving the house previously due to perceived social stigma from coughing, improvements in exercise tolerance, and reports enjoyment playing with her grandchildren again. Her cough severity index (CSI; scores ranging from 0 to 40) (Figure 1)[2] and cough visual analogue scale (VAS) taken pre- and post-commencement of HHFT improved from 38 to 14, and 100 mm to 15 mm (Figure 2) respectively. The reduction in VAS score was in excess of the minimal clinically important difference (MCID) of 30 mm.[1]

Case two

A 67-year-old never-smoking woman with idiopathic pulmonary fibrosis (IPF), was referred with progressive debilitating chronic cough for several years, particularly disruptive over the previous 12 months. She was initially diagnosed with unclassifiable ILD and treated with 12 months of oral prednisolone and mycophenolate mofetil, without benefit. A subsequent surgical lung biopsy demonstrated "usual interstitial pneumonia" on histopathology. She was diagnosed with IPF after multi-disciplinary team discussion. She was subsequently prescribed nintedanib. When she was referred to our service, her cough had not responded to nebulised lignocaine or gabapentin.

Lung function testing demonstrated restriction with FEV_1 of 1.5 L (70% predicted), and FVC of 1.72 L (63% predicted), and a normal DLco of 15.33 mL/min/mmHg (86% predicted). Her past medical history included mild sinusitis managed with saline nasal spray and intermittent intranasal steroids, and anxiety.

Her frequent disruptive paroxysms of dry cough were unrelenting, occurring both day and night, affecting daytime activities and sleep. She had associated frequent urinary incontinence due to cough, needing to wear incontinence pads. When first seen in clinic, she spoke in words and phrases limited by paroxysms of coughing. Her cough was triggered by smoke, strong odours, speaking, and movement. She reported dry eyes and mouth but no other clear features of a connective tissue disease (both clinically and on blood tests). There was subjective worsening in her voice quality without associated dysphagia, wheeze, nasal, or swallowing symptoms. She denied other symptoms of obstructive sleep apnoea.

Review by speech pathology suggested that her chronic cough was potentially secondary to an irritable larynx with specific triggers and intermittent dysphonia characterized by vocal strain. Subsequent nasoendoscopy by an otorhinolaryngologist showed a normal larynx with symmetrical vocal fold movement bilaterally, no features of reflux or oedema, and no clear evidence of vocal cord dysfunction.

She was commenced on HHFT (MyAIRVO™ system) using 15 L/min of air which resulted in almost immediate improvement in the frequency of her cough. Whilst using constant HHFT, she was able to maintain long periods cough-free and subsequent coughing episodes usually occurred in the setting of a significant trigger. She was able to remain mostly cough-free overnight with improved sleep. However, her cough returned within minutes after coming off HHFT.

Follow-up at 1 year demonstrated a stable clinical picture with ongoing good cough suppression with both daytime and nocturnal use of HHFT. She was no longer wearing incontinence pads. However, she continued to have persistent cough when not using HHFT. Her CSI and VAS reduced from 32 to 25, and 85 mm to 40 mm (Figure 2) (meeting MCID)[1] respectively. Whilst she was still largely house-bound, she was now allowing friends and family to visit where she had previously declined due to social embarrassment caused by her cough.

APPENDIX B

Cough Severity Index (CSI)

Name: _____
Date: ___ / ___/ ___

These are some symptoms that you may be feeling. Please circle the response that indicates how frequently you experience the same symptoms (0 = never, 1 = almost never, 2 = sometimes, 3 = almost always, 4 = always).

1. My cough is worse when I lie down.	0	1	2	3	4
2. My coughing problem causes me to restrict my personal and social life.	0	1	2	3	4
3. I tend to avoid places because of my cough problem.	0	1	2	3	4
4. I feel embarrassed because of my coughing problem.	0	1	2	3	4
5. People ask, "What's wrong?" because I cough a lot.	0	1	2	3	4
6. I run out of air when I cough.	0	1	2	3	4
7. My coughing problem affects my voice.	0	1	2	3	4
8. My coughing problem limits my physical activity.	0	1	2	3	4
9. My coughing problem upsets me.	0	1	2	3	4
10. People ask me if I am sick because I cough a lot.	0	1	2	3	4

FIGURE 1 Cough Severity Index questionnaire.[2]

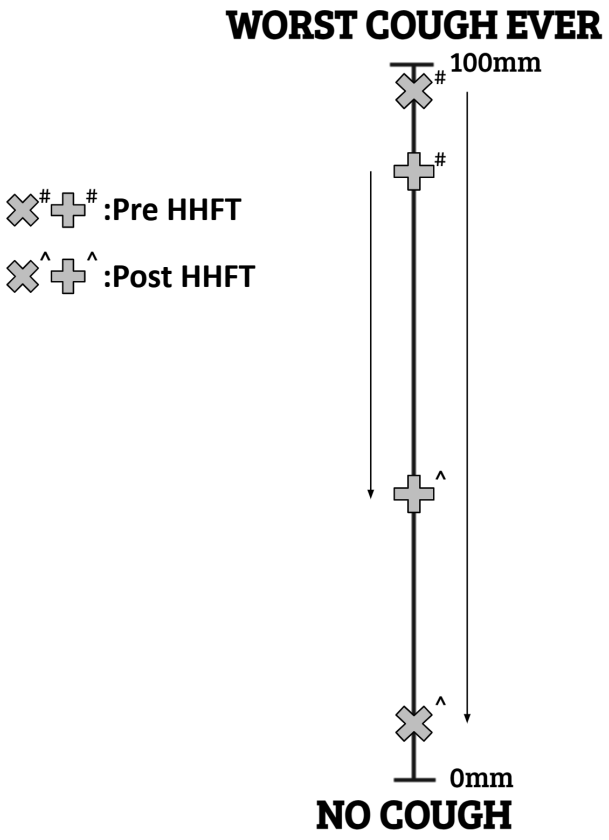

FIGURE 2 Cough Visual Analogue Scale as reported by patients. x: Case report one's responses before (#) and after (^) HHFT implementation. +: Case report two's responses before (#) and after (^) HHFT implementation.

DISCUSSION

Cough is a common symptom amongst people with ILD, with no effective treatments available. In addition, the mechanisms of cough generation in ILD are poorly understood.[3] HHFT has been shown to improve mucociliary clearance, dead space washout, and ventilation.[4] However, the role of HHFT for treating cough has not been well studied. In the case of the woman with primary Sjogren's disease (case 1), airway dryness was likely a significant contributor to her chronic cough. The patient's symptoms improved with a short trial of humidification suggesting that reducing airway dryness can provide immediate benefits in reducing cough. Notably, the effects of HHFT were long lasting, with a decrease in daytime cough and subsequent nocturnal cough despite intermittent long-term use of the therapy. Airway dryness alone has been shown to produce chronic airway neutrophilic inflammation and mucus obstruction.[5] This could explain the lasting effect of HHFT use. It is interesting to note she did not have a similar improvement with nebulised saline, suggesting both heat and humification are important. Airway dryness has also been shown to impair mucociliary clearance.[5] With decreased clearance comes increased airway irritants and therefore a greater activation of the cough reflex.

For the woman with IPF (case 2), the cough was only controlled when she utilized HHFT. In addition to the benefits of reducing airway dryness, it is possible that the delivery of a small amount of extrinsic positive end expiratory pressure (PEEP) may have led to the splinting of collapsible small airways.[5] Increasing PEEP is also likely to assist smaller airway secretion clearance by opening previously collapsed airways and thereby displacing mucus and assisting movement towards the pharynx. HHFT may also reduce chronic airway inflammation,[5] leading to reduction in the sensitivity of the cough reflex, and therefore the patient's propensity to cough.

Both described patients displayed significant improvement in cough and health-related quality of life with the use of HHFT. The two cases highlight the promising future of HHFT in chronic cough given the limited therapeutic options available to patients who suffer from this debilitating condition. Further research through a randomized clinical trial will be useful in validating the large-scale utility of HHFT in the chronic cough cohort.

AUTHOR CONTRIBUTIONS

Matthew Bricknell: Preparation of manuscript. **Chris Zi-Fan Zhao**: Preparation of manuscript. **Natasha Smallwood**: Preparation of manuscript. **Nicole Goh**: Treating clinician; preparation of manuscript.

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myAIRVO™ machines were provided by Fisher and Paykel.

CONFLICT OF INTEREST STATEMENT

Nicole Goh is an Associate Editor of Respirology Case Reports and a co-author of this article. She was excluded from all editorial decision-making related to the acceptance of this article for publication.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

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REFERENCES

1. Martin Nguyen A, Bacci ED, Vernon M, Birring SS, La Rosa C, Muccino D, et al. Validation of a visual analog scale for assessing cough severity in patients with chronic cough. Ther Adv Respir Dis. 2021;15:1–13.
2. Shembel AC, Rosen CA, Zullo TG. Development and validation of the cough severity index: a severity index for chronic cough related to the upper airway. Laryngoscope. 2013;123(8):1931–6.

3. Ryerson CJ, Abbritti M, Ley B, Elicker BM, Jones KD, Collard HR. Cough predicts prognosis in idiopathic pulmonary fibrosis. Respirology. 2011;16(6):969–75.
4. D'Cruz RF, Hart N, Kaltsakas G. High-flow therapy: physiological effects and clinical applications. Breathe. 2020;16(4):200224.
5. Vega ML, Schifino G, Pisani L, Nava S. Home high-flow therapy in patients with chronic respiratory diseases: physiological rationale and clinical results. J Clin Med. 2023;12(7):2663.

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