ORIGINAL RESEARCH LETTER

Nonpharmacological cough control therapy for chronic refractory cough and cough associated with underlying lung disease

To the Editor:

Cough is a common and frequently debilitating symptom. A persistent cough unresponsive to empirical treatment (chronic refractory cough (CRC)) or unexplained may represent a distinct phenotype [1]. The pathophysiology of CRC is poorly understood. "Cough hypersensitivity syndrome" has recently been the dominant paradigm. Evidence suggests a complex interplay of aberrant vagal afferent pathways [2] and central factors including impaired cough suppression [3]. Cough is more usually associated with an underlying cause (explained cough) and may persist in patients with underlying lung disease even after optimising treatment of the condition. Cough reflex hypersensitivity may be a specific treatable trait in airway disease [4]. Cough is common in asthma; studies demonstrate a link between airway dysfunction and cough hypersensitivity [5]. There are similar findings in bronchiectasis [6] and COPD [7], although the underlying mechanisms may differ.

In clinical practice, treatment of cases of persistent cough can be challenging. Medication such as morphine or gabapentin may be helpful but sometimes associated with significant side-effects and not all patients respond to drugs.

Our centre has extensive experience in cough control therapy (CCT), a complex, nonpharmacological intervention. CCT in CRC is supported by several uncontrolled case series and two small randomised controlled trials (RCTs) [8]. We have observed that many patients improve but a significant minority do not and we have no way of identifying nonresponders. The effectiveness of CCT in treating cough associated with underlying lung disease (explained cough) is unknown.

Clinical data prospectively gathered from patients undergoing CCT between 2013 and 2018 were reviewed. Appropriate local approval was obtained. Patients underwent a 3-month programme usually involving three 45-min appointments. The intervention is complex and described elsewhere [8]. Elements include education, vocal/laryngeal hygiene and hydration, cough control techniques, and psychoeducational counselling. Data are presented by type of cough (CRC and explained). Definitions of cough are controversial and lack consensus [9]; our CRC group comprised those with unexplained cough, and those who had not responded to empirical treatment and had no obvious underlying lung disease. "Explained" cough comprised patients with a persistent cough despite optimal treatment of underlying lung disease. Outcomes included a patient report (did their cough improve/not improve following CCT) and validated quality of life (Leicester Cough Questionnaire (LCQ) and symptom scores (Newcastle Laryngeal Hypersensitivity Questionnaire (LHQ)). Change in outcome scores post-treatment was only analysed in patients with a complete dataset and compared to the minimal clinically important difference (MCID) for each instrument. A response to CCT

@ERSpublications
Nonpharmacological cough control therapy (CCT) is effective for refractory chronic cough but there is a significant subgroup of nonresponders. CCT appears to be effective in cough associated with underlying disease such as asthma. http://bit.ly/2uCCwu3

Cite this article as: Mohammed S, Steer J, Ellis J Nonpharmacological cough control therapy for chronic refractory cough and cough associated with underlying lung disease. *ERJ Open Res* 2020; 6: 00243-2019 [https://doi.org/10.1183/23120541.00243-2019].

was defined as mean change in LCQ of at least the MCID (⩾1.3). A clinically significant change in LHQ was defined as a change of ⩾1.7. To describe the sample, proportions for categorical variables, means with standard deviations for parametric variables and medians with interquartile ranges for nonparametric variables are used. Bivariate comparisons using Student's t-test, Mann–Whitney U-test or Fisher's Exact test, where appropriate, were used to identify variables associated with lack of treatment response. SPSS version 21.0 (IBM, Armonk, NY, USA) was used for analysis of variables.

The CRC group comprised 228 patients, 170 (74.6%) of whom were female and 207 (90.8%) of whom had cough duration ⩾1 year. 132 (57.9%) had never smoked, 70 (30.7%) were ex-smokers and smoking status was unknown for 26 (11.4%). 212 patients had pre-treatment LCQ scores (mean±SD pre-treatment LCQ 12.18±3.6) and 172 patients had pre-treatment LHQ scores (pre-treatment LHQ 14.61±3.1).

The patient report (did cough improve/not improve following CCT) was available in 173 out of 228 patients (50 did not attend follow up and five could not complete treatment due to deteriorating health or were referred to other services). 148 (85.5%) out of 173 patients reported improvement; treatment did not improve cough in 25 (14.4%) out of 173 patients.

LCQ data pre- and post-treatment were available in 145 patients; total LCQ score improved by 4.55±3.41 and 120 (82.8%) patients achieved a change in total LCQ score of at least the MCID. 25 (17.2%) patients did not respond to CCT (mean change <1.3). Among those with pre- and post-LHQ data (n=115), there was an improvement in the mean total LHQ score by 2.87±2.63 and 72 (62.6%) patients had a change in total LHQ score of at least the MCID.

The explained cough group comprised 98 patients, 73 (74.5%) of whom were female and 88 (89.8%) of whom had cough duration ⩾1 year. 45 (45.9%) had never smoked, 49 (50%) were ex-smokers and smoking status was unknown for four (4.1%). 84 patients had pre-treatment LCQ scores (pre-treatment LCQ 11.36±4.12) and 75 patients had pre-treatment LHQ scores (pre-treatment LHQ 14.69±3.16). Underlying diagnoses were asthma in 58 (59.2%), COPD in 12 (12.2%), interstitial lung disease in seven (7.1%), bronchiectasis in 16 (16.3%) and xerotrachea in five (5.1%) (four patients with Sjögren disease and one with cutaneous systemic sclerosis).

The patient report (did cough improve/not improve?) was available for 74 out of 98 patients (20 (20.4%) patients did not attend follow-up and four (4.1%) could not complete treatment due to deteriorating health). 50 (67.6%) out of 74 patients reported improvement and treatment did not improve cough in 24 (32.4%) out of 74 patients.

LCQ data pre- and post-treatment were available in 57 patients; mean LCQ score improved by 3.76±5.07 and 39 (68.4%) patients had a change in total LCQ score of at least the MCID. 18 (31.6%) patients did not respond to CCT (mean change <1.3). Among those with pre- and post-LHQ data (n=51), there was an improvement in the mean total LHQ score by 2.34±3.03 and 28 (54.9%) patients had a change in score of at least the MCID (table 1).

There was no difference in baseline data between those with a complete and those with an incomplete dataset.

No factors (sex, smoking status, cough duration, age, or pre-treatment LCQ or LHQ score) were significantly associated with response to CCT in either group. Patients with a worse pre-treatment LCQ were more likely to respond to treatment (pre-treatment LCQ 12.06±3.13 in responders compared with

TABLE 1 Outcomes following cough control therapy (CCT) for patients with chronic refractory cough (CRC) and explained cough

Aetiology	LCQ				LHQ			
	Patients with pre- and post-CCT scores	Pre-CCT	Post-CCT	Change	Patients with pre- and post-CCT scores	Pre-CCT	Post-CCT	Change
CRC (n=228)	145	12.4±3.4	17.0±3.3	4.55±3.4	115	14.4±2.8	17.3±2.8	2.87±2.6
Explained cough (n=98)	57	11.6±3.6	15.4±4.3	3.76±5.1	51	14.6±3.0	16.9±3.2	2.34±3.0
Asthma (n=58)	36	11.3±3.3	15.6±4.4	4.27±4.8	33	14.6±3.2	16.9±3.6	2.24±3.2
COPD (n=12)	5	10.3±3.3	14.8±5.5	4.5±5.6	2	14.3±4.5	18.5±3.1	4.17±1.4
ILD (n=7)	3	12.7±2.2	16.2±3.4	3.51±4.1	3	14.8±2.7	18.2±1.7	3.33±2.0
Bronchiectasis (n=16)	9	12.1±4.8	14.5±4.5	2.41±6.8	11	14.1±2.7	16.3±2.7	2.14±3.5
Xerotrachea (n=5)	4	13.7±5.6	15.2±3.3	1.50±4.4	2	15.5±1.7	17.3±1.8	1.81±0.2

Data are presented as mean±SD unless otherwise stated. LCQ: Leicester Cough Questionnaire; LHQ: Laryngeal Hypersensitivity Questionnaire; ILD: interstitial lung disease.

13.76±4.37 in nonresponders, p=0.005) but this is likely to be a consequence of using mean change in LCQ as the definition of treatment response.

These are the first data to demonstrate improved patient outcomes when nonpharmacological CCT is used to treat cough associated with lung disease. We also report the largest series so far of patients undergoing CCT for CRC and demonstrate a significant "nonresponder" group.

There are limitations to this analysis; we used a clinical database reflecting "real-life" data. As such, there are missing data, some patients were lost to follow-up and not all had scores recorded at each visit. In the CRC group, the number of treatment nonresponders was fairly small, making it harder to identify variables to predict nonresponse. For patients with explained cough, some diagnostic groups were very small, limiting generalisability.

Most patients with CRC felt better, with improved symptoms and quality of life. CCT compares favourably to currently available drugs, with no known side-effects, and may be highly cost effective [10]. A significant subgroup does not respond who we cannot currently predict. Other studies suggest that associated breathing pattern disorder may predict response [11] but we were unable to examine this. In patients with CRC, CCT should be considered a safe and cost-effective first-line approach. This treatment should be regarded as a routine part of any respiratory service and not a specialised tertiary service. Efforts should be made to ensure CCT becomes much more widely available.

This analysis of clinical practice at our centre suggests CCT may be useful in patients with cough associated with underlying lung disease. Most of our explained cough patients had underlying asthma. A persistent cough refractory to standard asthma treatment is well recognised [4] and cough hypersensitivity may be an isolated treatable trait in patients with other airway disease. Patients may describe different "types of cough" and can differentiate an essential cough to clear secretions from cough hypersensitivity. CCT should not be used routinely in this group yet. Any intervention should be refined for this specific group and an RCT conducted to test the effectiveness and, in particular, the safety of this intervention; suppressing cough in patients with underlying airway disease may theoretically carry an increased risk of infection. We do not have sufficient data to confirm or refute this possibility.

Sana Mohammed[1], John Steer[1], Jenny Ellis[1,2] and Sean M. Parker[1]
[1]Respiratory Medicine, North Tyneside General Hospital, North Shields, UK. [2]Speech and Language Therapy, North Tyneside General Hospital, Northumbria Healthcare NHS Foundation Trust, North Shields, UK.

Correspondence: Sean M. Parker, Respiratory Medicine, North Tyneside General Hospital, Northumbria Healthcare NHSFT, North Shields, NE29 8NH, UK. E-mail: sean.parker@nhct.nhs.uk

Received: 11 Sept 2019 | Accepted after revision: 6 Feb 2020

Conflict of interest: None declared.

References

1 Gibson PG, Vertigan AE. Management of chronic refractory cough. *BMJ* 2015; 351: h5590.
2 Turner RD, Birring SS. Chronic cough: ATP, afferent pathways and hypersensitivity. *Eur Respir J* 2019; 54: 1900889.
3 Ando A, Smallwood D, McMahon M, *et al.* Neural correlates of cough hypersensitivity in humans: evidence for central sensitisation and dysfunctional inhibitory control. *Thorax* 2016; 71: 323–329.
4 Agusti A, Bel E, Thomas M, *et al.* Treatable traits: toward precision medicine of chronic airway diseases. *Eur Respir J* 2016; 47: 410–419.
5 Satia I, Watson R, Scime T, *et al.* Allergen challenge increases capsaicin-evoked cough responses in patients with allergic asthma. *J Allergy Clin Immunol* 2019; 144: 788–795.e1.
6 Torrego A, Haque RA, Nguyen LT, *et al.* Capsaicin cough sensitivity in bronchiectasis. *Thorax* 2006; 61: 706–709.
7 Belvisi MG, Birrell MA, Khalid S, *et al.* Neurophenotypes in airway diseases. insights from translational cough studies. *Am J Respir Crit Care Med* 2016; 193: 1364–1372.
8 Chamberlain Mitchell SAF, Ellis J, Ludlow S, *et al.* Non-pharmacological interventions for chronic cough: the past, present and future. *Pulm Pharmacol Ther* 2019; 56: 29–38.
9 McGarvey L, Gibson PG. What is chronic cough? Terminology. *J Allergy Clin Immunol Pract* 2019; 7: 1711–1714.
10 Birring SS, Floyd S, Reilly CC, *et al.* Physiotherapy and speech and language therapy intervention for chronic cough. *Pulm Pharmacol Ther* 2017; 47: 84–87.
11 Chamberlain Mitchell SA, Garrod R, Clark L, *et al.* Physiotherapy, and speech and language therapy intervention for patients with refractory chronic cough: a multicentre randomised control trial. *Thorax* 2017; 72: 129–136.