


Management of cough in patients with idiopathic interstitial lung diseases in primary care

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Abstract

Importance: Cough is a common symptom in idiopathic interstitial lung diseases (ILDs), there is little information of its management in primary care. The objective of this study was to explore the frequency of cough-related consultations and the medications prescribed to patients with ILDs in primary care. **Methods:** This retrospective cohort study used electronic medical records (EMR) from Manitoba primary care providers participating in the Manitoba Primary Care Research Network repository (2014–2019). Cough-related consults and the subsequent medications prescribed to patients with ILDs were identified in the EMR. **Results:** 295 patients with ILDs were identified, 73 (25%) of them had 141 cough-related consultations (mean 1.9, SD 1.3) during the period studied. In 50 (35%) of the consultations, patients were prescribed one or more of the following: inhaled bronchodilators (34%), nasal corticoids (18%), codeine/opiates (18%), antibiotics (14%), inhaled corticoids (14%), proton pump inhibitors (8%), cough preparations (6%), antihistamines (4%), and oral corticoids (2%). 13 (26%) subsequent cough-related consultations were identified within 6 months, mainly among patients who were prescribed cough preparations, nasal corticoids, antihistamines, and antibiotics. **Conclusion:** One-quarter of patients with ILDs consulted primary care due to cough, and about a third of them received a prescription to address potentially underlying causes of cough. Although further studies are required to explore the effect of the medications prescribed, recurrent cough consultations suggested that cough preparations, nasal corticoids, and antihistamines are among the least effective treatments. More research is needed to understand the causes and optimal treatment of cough in patients with ILDs.

Keywords

idiopathic interstitial lung diseases, chronic cough, primary care, cough management, pulmonary fibrosis

Key Points

- One-quarter of patients with ILDs consulted primary care due to cough, and about a third of them received a prescription to address potentially underlying causes.
- Inhaled bronchodilators were the most prescribed drug followed by nasal corticoids and opiates.
- Recurrent cough consultations suggested that cough preparations, nasal corticoids, and antihistamines are among the least effective treatments.

strive to diagnose and manage, when possible, the underlying cause of presented symptoms. However, clinical uncertainty can lead to symptom-focused primary care consults.² Retrospective reviews of medical records indicate that prior to

Background

Coughing is one of the most common reasons for patient consultation in primary care settings.¹ Primary care providers

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referral for specialized care, many patients with chronic cough undergo empirical trials of treatment in primary care settings (e.g., cough syrup, inhaled corticosteroids, inhaled bronchodilators, treatment for gastro-esophageal reflux). In addition to limited clinical benefits, empirical trials may also result in patients being exposed to the risk of medication-related adverse events,¹ especially if patients have multiple comorbidities and medications.

The term idiopathic interstitial lung diseases (ILDs) combines a wide range of lung disorders of unknown cause that distort the lung parenchyma with inflammation and fibrosis. Prevalence of chronic cough in ILDs has not been established. However, it was reported in up to 80% of patients with idiopathic pulmonary fibrosis (IPF), which is one of the most common ILDs.^{2–4} Evidence indicated that severe cough, mostly dry with a diurnal pattern, can have a major impact on the physical, mental and social health and quality of life (QoL) of the patient.^{5,6}

The causes of chronic cough in patient with ILDs have not been fully elucidated. Many studies suggest that the pathogenesis of cough in these patients is likely “multi-factorial,” influenced by architectural distortion of the lungs, increased cough reflex sensibility, genetic factors and/or inflammation.⁷ In addition, it is hypothesized that co-existing comorbidities such as upper airway cough syndrome (UACS), asthma, chronic obstructive pulmonary disease (COPD), and gastro-esophageal reflux disease (GERD), may have an important role.^{6,7}

The management of cough in patients with ILDs in clinical practice is a major challenge, as it is often refractory, and there are not proven treatments available. Therefore, current approaches focus on addressing possible comorbidities. Overall, there is little information about the management of cough in patients with ILDs in primary care. Therefore, the objective of this study was to explore cough-related consultations and medications prescribed to patients with ILDs in primary care.

Methods

This retrospective study used electronic medical records (EMR) from Manitoba primary care providers participating in the Manitoba Primary Care Research Network (MaPCReN). Manitoba primary care research network extracts EMR data from consenting family physicians, nurse practitioners, and community pediatricians. The MaPCReN is the Manitoba provincial-based research network within the Canadian Primary Care Sentinel Surveillance Network (CPCSSN) database. The CPCSSN merges extracts from each provincial-based research network into a pan-Canadian EMR data repository. Canadian primary care sentinel surveillance network and each of the provincial practice-based networks have developed an advanced infrastructure, set of tools and highly automated processes for extracting,

processing and analyzing EMR information from primary care practices across Canada. On 31 December 2019 MaPCReN contains information extracted from 53 primary care clinics, representing 256 providers who care for 289,559 patients in Manitoba. This study approved by the Health Research Ethics Board of the University of Manitoba (HS23882) used data representing patient details, billing records, encounter diagnoses, problem lists, and prescribed medications derived from provider EMRs.

Study setting

Manitoba is one of the three prairie provinces of Canada with a population of 1,386,938 million (57% in Winnipeg) in 2020.⁸ MaPCReN represents 21% of the Manitoba population. Canada maintains a universal, publicly funded healthcare system that provides Manitobans’ access to health care services. The provincial Pharmacare program will cover the cost of some prescribed medications for Manitoba residents who spend a large amount of their income on medications, following payment of the income-based deductible.

Study population

The data was extracted from the MaPCReN repository (2019-Q4, 31 December 2019) for the years 2014–2019. Patients with at least one appointment to a MaPCReN provider between 1 January 2014 and 31 December 2019 were included. Patients with diagnosis of ILDs were identified in the database by International Classification of Disease (ICD-9-CM) code-based algorithm that required individuals to be over 18 years of age and to have at least one record for ICD-9 codes 515 (Pulmonary congestion and hypostasis), 516.3 (Idiopathic fibrosing alveolitis), 516.31(IPF) in the billing or problem list of the EMR.⁹

Outcome measures

Cough-related consultation in ILDs patients were identified using the ICD-9 code 786.2 in the billing table of the EMR. Medications prescribed: Disease specific antifibrotic medications are usually prescribed by specialist and not in primary care. Therefore, the present study focused on exploring prescriptions commonly used to treat potentially contributing factors of cough.^{3,10,11} Anatomical Therapeutic Classification (ATC) codes were used to identify cough preparations (R05), antihistamines (R06AA), nasal preparations (R01AX), nasal corticosteroids (R01AD), oral corticoids (H02), antibiotics (J01), opiates (N02AA), inhaled bronchodilators (R03A), inhaled corticoids (R03B), and proton pump inhibit (PPI) therapy (A02BC) within a week after a cough-related consultation. Among patients with a prescription for a cough-related consultation we assessed for a subsequent cough-related consultation within the following

6 months after an initial consultation date as a potential indicator of ineffective treatment. Cough-related consultations beyond 6 months were accounted as a new episode.

Analysis

Descriptive statistics were used to present the participants. Percentages were used for categorical variables and means (standard deviations (SDs)) for continuous variables. Chi-squared tests were used to compare medications prescribed between groups. Statistical significance was accepted at p -values < 0.05. All analyses were performed using SPSS software, version 24.0 (SPSS, Chicago, IL, USA).

Results

Table 1 shows that 295 out of the 194,540 (151.6 per 100,000) patients who had an appointment to a primary care provider participating in MaPCReN between 1 January 2014 and 31 December 2019 had a diagnosis of ILDs. Patients with ILDs were significantly older (74.5 years (SD 13.9) vs. 41.3 years (SD 25.2), p -value < 0.0001) and received more prescriptions for the drugs explored in this study (68.8% of patients with ILDs received ≥ 1 medication compared to 34.1% of patients without ILDs (p -value < 0.0001)). 25% (73/295) of the patients with ILDs had one or more cough-related consultation during the period studied. Idiopathic interstitial lung diseases

patients with cough-related consultation were significantly ($p = 0.02$) younger (mean 71.2, SD 15.0 years) than ILDs patients without it (mean 75.3, SD 13.3 years). Analyses of medications prescribed to ILDs patients at any time during the study period indicated that patients with cough-related consultations received more prescriptions for antihistamines (16.4 vs 6.3%), codeine/opiates (43.8% vs. 31.1%), nasal steroids (39.7% vs. 20.7%), inhaled bronchodilators (57.5% vs. 40.5%), and inhaled corticosteroids (34.2% vs. 22.5%) (Table 1).

141 cough-related consultations (mean 1.9, SD 1.3) were identified in patients with ILDs during the period studied. Table 2 shows that 59 medicines were prescribed in 35.4% (50/141) of these consultations. Inhaled bronchodilators were the most prescribed (34.0%) followed by nasal corticoids (18.0%) and opiates (18.0%). Combination of more than one medicines were prescribed in 7 consultations. 13 subsequent cough-related consultations were identified within 6 months. Recurrent cough consultation occurred mainly among patients who were prescribed cough preparations (66.7%), nasal corticoids (55.5%), antihistamines (50.0%), and antibiotics (42.8%).

Discussion

Electronic medical records showed that 1 in 4 patients with ILDs consulted primary care due to cough, and about a third

Table 1. Patients with an appointment to a primary care provider participating in MaPCReN between 2014 and 2019 (N = 194,540).

Variable	Patients without ILDs n = 194,245	Patients with interstitial lung diseases (ILDs) n = 295				p-value
		All	No cough appointment (2014–2019) n = 222	Cough appointment (2014–2019) n = 73	p-value	
Female patient (vs. male patient)	103,823 (53.5%)	147 (49.8%)	105 (47.3%)	42 (57.5%)	0.13	0.2125
Patient age, mean (SD)	41.3 (25.2)	74.5 (13.9)	75.6 (13.3)	71.2 (15.0)	0.02	<0.0001
Cough visit (2014–2019)	11,999 (6.2%)	73 (24.8%)	—	—		<0.0001
Medication prescribed* (2014–2019)						
Cough preparations	4151 (2.1%)	25 (8.5%)	16 (7.2%)	9 (12.3%)	0.17	<0.0001
Antihistamines	5316 (2.7%)	26 (8.8%)	14 (6.3%)	12 (16.4%)	<0.01	<0.0001
Decongestants/nasal sprays	4398 (2.3%)	18 (6.1%)	12 (5.4%)	6 (8.2%)	0.38	<0.0001
Nasal corticosteroids	26,360 (13.6%)	75 (25.4%)	46 (20.7%)	29 (39.7%)	<0.01	<0.0001
Inhaled corticosteroids	13,547 (6.9%)	75 (25.4%)	50 (22.5%)	25 (34.2%)	0.04	<0.0001
Oral corticoids	6809 (3.5%)	28 (9.5%)	18 (8.1%)	10 (13.7%)	0.16	<0.0001
Proton pump inhibitors (PPIs)	26,554 (13.7%)	102 (34.6%)	75 (33.8%)	27 (37.0%)	0.62	<0.0001
Inhaled bronchodilators	29,209 (15.0%)	132 (44.8%)	90 (40.5%)	42 (57.5%)	0.01	<0.0001
Opiates	17,122 (8.8%)	101 (34.2%)	69 (31.1%)	32 (43.8%)	0.04	<0.0001
Antibiotics	33,327 (17.2%)	69 (23.4%)	48 (21.6%)	21 (28.8%)	0.21	0.0046
COPD	5366 (2.8%)	86 (29.2%)	68 (30.6%)	18 (24.7%)	0.33	<0.0001
Asthma	23,070 (11.9%)	59 (20.0%)	38 (17.1%)	21 (28.8%)	0.03	<0.0001
Visit frequency, mean (SD)	3.0 (4.1)	8.3 (9.9)	7.6 (9.3)	10.1 (11.4)	0.07	<0.0001

*Medications prescribed at any time during the study period, not necessary after a cough visit.

Table 2. Medications prescribed to patients with Interstitial Lung diseases (ILDs) after a cough-related consultation to primary care and a subsequent cough-related consultation.

Medications prescribing in consultations	Subsequent cough consultation (<6 months)	
Name	% (times prescribed/ consultations x 100)	% (subsequent cough consultations/ times prescribed x 100)
All prescriptions		
Cough preparations	6.0	66.6
Antihistamines	4.0	50.0
Decongestants/nasal sprays	0.0	0.0
Nasal corticosteroids	18.0	55.5
Inhaled corticosteroids	14.0	14.2
Oral corticoids	2.0	0.0
Proton pump inhibitors (PPIs)	8.0	0.0
Inhaled bronchodilators	34.0	11.7
Opiates	18.0	22.2
Antibiotics	14.0	42.8
Total	100	—
More than one medication prescribed in 7 consultations		
Cough Preparations+ antibiotics	2.0	100
Codeine/Opiates+ inhaled bronchodilators	2.0	0
Codeine/Opiates+ nasal corticosteroids	2.0	0
Inhaled bronchodilators + oral Corticoids+ Antibiotics+ proton pump inhibitors (PPIs)	2.0	0
Inhaled Bronchodilators+ antihistamines	2.0	100
Inhaled bronchodilators + proton pump inhibitors (PPIs)	2.0	0
Nasal Corticosteroids+ inhaled corticosteroids	2.0	0

50 cough-related consultations received 59 prescriptions. In 14% (7/50) of the consultations, patients were prescribed more than one medication. Numbers were suppressed due to low occurrences.

of them received a prescription to address potentially underlying causes. To the best of our knowledge, this is the first study that explored the prevalence of cough-related consultation and management of cough among patients with ILDs in primary care.

Cough preparations were prescribed in 6% of the consultations, a subsequent cough consultation was reported in two third of them within the subsequent 6 months. This aligns with previous evidence which reported that conventional antitussive therapy is often not beneficial.⁶ Antihistamines and nasal corticosteroids were prescribed in 4% and 18% of the cough consultations, respectively, and a subsequent cough appointment was identified in over half of them. Antihistamines and nasal corticoids are commonly used to treat upper respiratory cough syndrome (UACS), previously referred as postnasal drip syndrome, which is considered one of the most common causes of chronic cough.^{11,12} It is believed that nasal and inhaled corticosteroids may decrease coughing by reducing inflammation and opening the airways,¹³ but their effect has not been

studied in ILDs. Oral corticoids were prescribed only in 2% of the consultations in the present study. A recent study⁶ found evidence to suggest that oral corticoids help improve cough symptoms in IPF. However, no effect on QoL was found and possible side-effects should be taken into consideration.⁶ Proton pump inhibitors (PPIs) were prescribed in 8% of the consultations. Gastro-esophageal reflux disease may contribute to or exacerbate cough in IPF patients.¹⁴ It has been suggested that PPI therapy can be used to treat GERD-related cough, however, there is conflicting evidence of its effectiveness.^{15,16}

Inhaled bronchodilators were the most frequently prescribed medication after a cough-related consultation in our study. Although there is no evidence of the effectiveness of inhaled bronchodilator for the management of cough in patients with ILDs,^{14,17} a subsequent cough-related consultation occurred only in 11.7% of patients who received this prescription, which may suggest some benefit. Opiates were prescribed in 18% of the consultations. Opioid therapy can be beneficial in refractory cough in pulmonary fibrosis.¹² A

study shown a positive effect of opiates on chronic intractable cough, probably due to an antitussive effect via neuro-modulators.¹⁸ However, there are reservations about the recommended use of opiates for the management of cough, primarily due to concerns regarding their influence in the protective mechanism of cough, potential abuse and long-term effects.^{6,19}

Antibiotics were prescribed in 14% of the consultations; a subsequent consultation was registered in 42.8% of them within the following month. Although these may be needed to treat cough caused by a respiratory tract infection, evidence suggested that antibiotics do not seem to improve cough severity and QoL in patients with IPF and adverse effects were more likely to be observed.²⁰

There is little evidence on commonly prescribed cough treatments for ILDs patients and their effectiveness, and existing studies have focused on IPF. It has been proposed that addressing potential comorbidities may help those ILD patients who experience a significant impact of coughing on their QoL; however, the existing evidence is not yet conclusive. In the present study, recurrent cough consultations suggested that cough preparations, nasal corticoids, and antihistamines may be less effective treatments. However, more research is needed to understand the cause and effect of cough treatment in ILDs. This should include analysis of encounter notes documenting clinical presentation, discussion with the patient, as well as clinical assessments and investigations providing details related to treatment decisions.

Limitations and strengths

Several limitations of this study should be considered when interpreting the results. First, although data included in this study represent a comprehensive sample of primary care appointments in Manitoba, the MaPCReN database only includes consenting PCPs in Manitoba, representing approximately 20% of Manitoba providers. Second, it is possible that the prevalence of cough-related consultations may have been over- or underestimated due to inconsistencies in codes recorded in the EMR if cough was not considered the main reason for consultation. Third, the absence of a subsequent cough appointment could be due to an improvement in cough symptoms, a lack of proper coding, or obtainment of secondary care. Therefore, the authors prefer to be cautious and refrain from stating which treatments seem to provide better results in the management of cough in ILDs. Fourth, prescribing practices may have been influenced by specific patients' characteristics, and by provider and/or patient preferences. Fifth, this study only used structured data files available within the EMR and not clinic encounter notes, which may have provided more details related to treatment decisions (e.g., clinical presentation, discussion with the patient, clinical assessments and investigations). Finally, this study was based on EMRs

that may have some gaps in terms of data completeness,^{21,22} but using clinical data from EMRs has been shown to be valid for use in diagnoses.^{23,24} The use of good-quality EMR data from the MaPCReN database is one of the main strengths of this study. Furthermore, this is the first studies exploring the prevalence of cough-related consultation and management of cough among patients with ILDs in primary care. To expand this research, future studies should link primary care EMR data with data representing appointments to an allied health professional to assess the management of cough among patients with ILDs using non-pharmaceutical interventions.

Conclusions

One-quarter of patients with ILDs consulted primary care due to cough, and about a third of them received a prescription to address potentially underlying causes. Although further studies are required to explore the effect of the medications prescribed, our study suggests that cough preparations, nasal corticoids, and antihistamines are associated with recurrent cough consultations. More research is needed to understand the causes and optimal treatment of cough in patients with ILDs. Results contributed to closing an important knowledge gap on the current management of cough in patients with ILDs in primary care.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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