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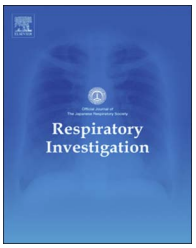

Original article

Gastroesophageal reflux symptoms and nasal symptoms affect the severity of bronchitis symptoms in patients with chronic obstructive pulmonary disease

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ABSTRACT

Background: Cough and sputum production (symptoms of bronchitis) are common in chronic obstructive pulmonary disease (COPD). Extrapulmonary comorbidities, such as gastroesophageal reflux disease (GERD) and post-nasal drip, also cause bronchitis symptoms. The impact of extrapulmonary comorbidities on the severity of bronchitis symptoms in COPD is unknown. The aim of this study was to quantify bronchitis symptoms and assess the impact of GERD and nasal symptoms on the severity of bronchitis symptoms in COPD.

Methods: In this cross-sectional study, stable COPD patients were recruited and completed the COPD assessment test (CAT) and Cough and Sputum Assessment Questionnaire (CASA-Q) to quantify bronchitis symptoms. To evaluate extrapulmonary comorbidities, the Frequency Scale for Symptoms of GERD (FSSG) questionnaire and nasal symptom questionnaire were completed. The impact of these comorbidities on the severity of bronchitis symptoms was analyzed.

Results: Ninety-nine COPD patients were recruited. The presence of GERD symptoms (24.2% in the study population) was associated with more sputum symptoms. The presence of nasal discharge (43.4%) was associated with more cough and sputum symptoms, whereas post-nasal drip (13.1%) was associated with more sputum symptoms. On multivariate analyses, nasal discharge was associated with more cough symptoms. GERD and post-nasal drip were associated with more sputum symptoms.

Abbreviations: BMI, body mass index; CASA-Q, Cough and Sputum Assessment Questionnaire; CAT, COPD assessment test; CB, chronic bronchitis; COPD, chronic obstructive pulmonary disease; CT, computed tomography; DL_{CO}, diffusion capacity of carbon monoxide; FEV1, forced expiratory volume in one second; FSSG, Frequency Scale of Symptoms of GERD; GERD, gastroesophageal reflux disease; LAA, low attenuation area; WA, airway wall area

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Conclusion: This study showed that the presence of GERD and/or nasal symptoms is associated with an increase in bronchitis symptoms. Careful assessment of extrapulmonary comorbidities is necessary in the evaluation of bronchitis symptoms in COPD patients.

1. Introduction

Cough and sputum production (symptoms of bronchitis) are common in chronic obstructive pulmonary disease (COPD) [1]. It is important to identify these symptoms because they are established risk factors for worse clinical outcomes in patients with COPD [1–3]. Moreover, COPD patients with cough and sputum production are reportedly more responsive to specific modes of therapy [4,5].

Cough and sputum occur due to various pathophysiological mechanisms. Productive cough may be due to airway mucus hypersecretion [6,7], whereas non-productive cough may result from increased cough sensitivity or bronchoconstriction due to increased airway sensitivity [8]. In addition to these pathophysiological mechanisms involving the airway, extrapulmonary causes of cough, such as gastroesophageal reflux disease (GERD) and post-nasal drip, also account for a large proportion of chronic cough cases [9,10].

GERD may cause chronic cough in two ways [11]. It may cause direct stimulation of the cough reflex in the upper respiratory tract; if the refluxate is aspirated, it might stimulate the lower respiratory tract, leading to cough. The other mechanism is by stimulation of the esophageal-bronchial cough reflex. This occurs when the distal esophagus is stimulated by the refluxate. The major mechanism by which nasal pathology causes bronchitis symptoms is by direct passage of the nasal discharge into the larynx (post-nasal drip), which stimulates the cough reflex [12]. Based on the concept of "one airway, one disease," stimulation at one point results in an inflammatory response throughout the airways.

Although these extrapulmonary comorbidities are frequent in COPD patients [13–15], little attention has been paid to the pathophysiological basis of cough and sputum production, especially due to extrapulmonary etiology. The extent to which extrapulmonary comorbidities affect the severity of bronchitis symptoms in COPD patients has not been elucidated.

To explore the impact of extrapulmonary comorbidities on the severity of bronchitis symptoms in COPD patients, we performed a questionnaire-based assessment of GERD and nasal symptoms. We carried out this evaluation using two questionnaires: the COPD Assessment Test (CAT) [16] and the Cough and Sputum Assessment Questionnaire (CASA-Q) [17].

2. Materials and methods

2.1. Study subjects and design

This cross-sectional study was conducted as part of a prospective observational study carried out at the Kyoto University Hospital [18]. We recruited 99 patients consecutively with stable COPD diagnosed according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria, from March 2013 through February 2014, from our outpatient clinics. Detailed inclusion and exclusion criteria are available in the online data supplement. The ethics committee of Kyoto University approved the present study (March 12, 2009, approval No. E182), and all patients provided written informed consent prior to study participation.

2.2. Quantification of cough and sputum symptoms

For the quantitative assessment of cough and sputum symptoms, patients completed the CAT [16] and the CASA-Q [17]. The CAT questionnaire has 8 items, including cough (item 1) and sputum (item 2), on a 6-point scale (0–5). In addition to the total scores, we recorded the scores on cough (CAT1) and sputum (CAT2). The CASA-Q is a validated questionnaire for evaluating cough and sputum symptoms in chronic bronchitis (CB) and COPD patients [17,19]. It includes 20 items on a 5-step scale and is divided into 4 domains, including cough symptom (COUS), sputum symptom (SPUS), cough impact (COUI), and sputum impact (SPUI)). The score in each domain ranges from 0 to 100, with a lower score indicating more severe symptoms or a higher impact. Patients were also questioned regarding the presence of classic CB symptoms as defined by the Medical Research Council [20] (cough and sputum for 2 or more consecutive years).

2.3. GERD evaluation

GERD symptoms were evaluated using the Frequency Scale for Symptoms of GERD (FSSG) questionnaire [21] as previously described [14].

2.4. Evaluation of nasal symptoms

Patients were asked about the presence of five nasal symptoms, including nasal discharge, nasal congestion, decreased sense of smell, post-nasal drip, and sneezing [22]. Nasal symptoms experienced on a regular basis were identified, while those occurring during a common cold or exacerbations were excluded.

Methods used for pulmonary function testing and CT acquisition and analysis are provided in the online data supplement.

2.5. Statistical analysis

All statistical analyses were performed with JMP 10 software (SAS Institute; Cary, NC). The relationship between two variables was assessed with the Spearman rank correlation test. Differences between two groups were evaluated by the Wilcoxon signed-rank test. For the evaluation of the relative

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