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Development and validation of a cough and sputum assessment questionnaire

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Summary
Although cough and sputum production may impact patients' well being and functioning in COPD and chronic bronchitis, there is no validated instrument for cough and sputum symptoms and their impact on patients' daily activities. To fill that gap, we developed and validated a specific, multilingual Cough and Sputum Assessment Questionnaire (CASA-Q) that evaluates clinical symptoms and their impact on patients with COPD or chronic bronchitis.

In a three-country validation study ($n = 671$), there was adequate internal consistency (Cronbach's alphas, 0.80–0.91) and test–retest reliability (correlation coefficients > 0.70) for the CASA-Q. The cough impact and sputum impact domains correlated with the SGRQ impact domain and SGRQ total score, as did the cough impact domain with the SF-36 social functioning domain. The cough symptom and sputum symptom domains correlated with sputum wet weight ($p < 0.05$; $r = -0.56$), but not with cough recordings. The mean CASA-Q cough symptom and sputum symptom domain scores indicated responsiveness towards both worse and improved symptoms, whereas the impact domains scored already in the upper third of the scale range, indicating the need for further improvement of its properties. Differences

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in the CASA-Q domain scores by smoking status (current vs. former smokers) were highest for cough symptoms and lowest for sputum impact. These data indicate that the CASA-Q may be a useful measure of cough and sputum production, and their impact in patients with COPD and/or chronic bronchitis. Further validation will need to assess the responsiveness of the CASA-Q to changes in symptoms.

Introduction

Airway mucus hypersecretion is a phenotype associated with several chronic inflammatory airway diseases, e.g., asthma and chronic bronchitis. The term ''chronic bronchitis'' originated from a clinical diagnosis usually defined by cough and sputum production on most days during three consecutive months for more than two successive years.[1] According to the current nomenclature used for chronic obstructive airway diseases, chronic obstructive bronchitis is subsumed under the disease entity of chronic obstructive pulmonary disease (COPD), which also includes emphysema.[2] COPD is characterized by airflow limitation that is not fully reversible, and is usually progressive. Sputum expectoration has been found to correlate with the decline in lung function in patients with COPD,[3] and a recent study indicated that the presence of cough and phlegm might identify subjects with a high risk of COPD.[4]

Cough and sputum production may be important contributors to patients' impaired well being and functioning in patients with COPD and chronic bronchitis. These symptoms and their impacts are therefore compelling outcomes to investigate from a patient perspective. Currently, there is no instrument that comprehensively measures cough and sputum symptoms and their impact on everyday life, specifically in this patient population. Several instruments have been developed to assess cough, including the Leicester Cough Questionnaire (LCQ), the Breathlessness, Cough and Sputum Scale (BCSS), the Cough-Specific Quality of Life Questionnaire (CQLQ), the Chronic Bronchitis Symptoms Assessment Scale (CBSAS), and the Chronic Cough Impact Questionnaire (CCIQ). The LCQ was developed for patients with chronic cough, however, it is unknown if any COPD patients were included in the development and therefore, it is not known if this questionnaire would be applicable to a COPD population.[5] Additionally, the LCQ focuses on three domains (physical, psychological and social), and not on sputum production or its impact. The BCSS was developed for COPD patients to track the severity of respiratory symptoms.[6] This three-item questionnaire was well developed, but asks solely about the frequency of cough rather than its impact making it less desirable if the goal is to assess both. The CQLQ was developed for patients with chronic cough, but lacked patient input during the development of the instrument.[7] The demographics of patients during the validation process included mostly post-nasal drip syndrome (81%) and gastro-esophageal reflux disease (72%), with less than 6% of the sample having chronic bronchitis. The CBSAS is well developed and validated, but is primarily focused on severity of cough and associated symptoms, such as shortness of breath, and lacks an adequate assessment of sputum and its impact.[8] The CCIQ was developed for patients with chronic cough, primarily focusing on post-nasal drip syndrome and gastro-esophageal reflux disease.[9] Given the lack of focus on cough and sputum impact, the aforementioned questionnaires were not appropriate for use in trials assessing cough and sputum production in patients with COPD or chronic bronchitis.

This study set out to develop and validate a specific Cough and Sputum Assessment Questionnaire for patients with chronic (obstructive) bronchitis, especially in accordance with the relevant guidelines set forth by regulatory agencies.[10,11] These guidelines define a Patient-Reported Outcome (PRO) as the ''measurement of any aspect of a patient's health status that comes directly from the patient (i.e., without the interpretation of the patient's responses by a physician or anyone else)''.[11] In order for an instrument to be considered well developed, the new guidelines have specified several key points. The development of the instrument must include patient involvement to assist in developing the concepts to be measured or, as the guidelines infer, the question generation process would be incomplete. A wide range of patients should be included in the development of a questionnaire to ensure a representative sample and variations in population characteristics. Following the development of the questions, it is important to review these questions with patients to ensure their clarity and relevance. A questionnaire is not considered valid until the statistical properties have been tested. The new guidelines direct researchers on the validation steps to ensure the measurement properties are adequate for use in clinical trials. Regulatory agencies want to be sure the questionnaire reliably measures the concepts it was designed to measure. It should be noted, however, that the statistical testing of the questionnaire should guide the development and not dictate which items remain in the questionnaire. Relevance to the patient and clinical importance should always be considered. Following these guidelines, we aimed to develop the questionnaire simultaneously in several languages from diverse geographical regions to ensure maximal cultural applicability.

Methods

Development phase

Conceptual framework

Literature and Patient-Reported Outcome (PRO) questionnaire reviews were conducted to assess the impact of cough and sputum on patients' lives and identify/appraise existing instruments. The data indicated that existing questionnaires did not satisfy all criteria (i.e., they were nonspecific for patients with COPD and chronic bronchitis, and/or had no patient involvement in questionnaire development). Thus, we developed a new PRO