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Evaluation of the psychometric properties of the St George's Respiratory Questionnaire in patients with severe asthma

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ABSTRACT

Purpose: Limited data exist on the quantitative validity of the St George's Respiratory Questionnaire (SGRQ) in asthma populations. This study evaluated the psychometric properties of the SGRQ in patients with severe asthma.

Methods: This was a post-hoc analysis of pooled data from MENSA (N = 576; NCT01691508) and SIRIUS (N = 135; NCT01691521), two randomized, placebo controlled trials of mepolizumab in patients with severe asthma. Patients completed the SGRQ at Baseline and Exit (MENSA Week 32; SIRIUS Week 24). Distributional characteristics, internal consistency reliability, test-retest reliability, convergent and discriminant validity, known-groups validity and responsiveness were assessed.

Results: Internal consistency reliability was acceptable for the total and domain scores at Baseline and Exit (Cronbach's α was 0.92 and 0.94 at Baseline and Exit, respectively, for the total score). Test-retest reliability was demonstrated (intraclass correlation coefficients >0.7) for total score and the Activity and Impacts domains. Convergent and discriminant validity were demonstrated with measures associated or not associated with respiratory-related health status. Known groups validity based on baseline FEV_1% predicted, Asthma Control Questionnaire (ACQ)-5 score, exacerbations and eosinophil counts was demonstrated for the SGRQ total and domain scores. Responses to therapy based on clinician-rated response, patient-rated response, ACQ-5 change score and exacerbations generally correlated with improvements in SGRQ scores.

Conclusions: This analysis demonstrated that the SGRQ has acceptable psychometric properties in patients with severe asthma, exceeding the thresholds for adequate reliability, validity and responsiveness. The SGRQ appears to be a good instrument for identifying response to therapy in patients with severe asthma.

1. Introduction

Established clinical measures of asthma severity, such as lung function and exacerbation rate, are used routinely to monitor changes in patients' condition and responses to therapy. Although such measurements provide valuable information, some key

Abbreviations: ACQ-5, Asthma Control Questionnaire-5; ANCOVA, analysis of covariance; ANOVA, analysis of variance; BDI-II, Beck Depression Inventory-II; CFA, confirmatory factor analysis; CFI, comparative fit index; COPD, chronic obstructive pulmonary disease; EMA, European Medicines Agency; EQ-5D, EuroQoL 5-D; FDA, Food and Drug Administration; FEV, forced expiratory volume; FVC, forced vital capacity; GINA, Global Initiative for Asthma; ICC, intraclass correlation coefficient; ICS, inhaled corticosteroids; IV, intravenous; OCS, oral corticosteroids; PRO, patient-reported outcome; RMSEA, root mean square error of approximation; SC, subcutaneous; SD, standard deviation; SF-36, Short-Form 36-item health survey; SGRQ, St George Respiratory Questionnaire; SRMR, standardized root mean residual; WPAI-GH, Work Productivity and Activity Impairment Questionnaire: General Health.

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symptoms of the disease (e.g. breathlessness, cough) can only be evaluated by patient-reported outcome (PRO) measures of health status. PROs can provide critical information about disease control, disease burden and treatment effectiveness when combined with clinical measures of asthma severity. PROs, therefore, are routinely measured in asthma clinical trials because they contribute to a more complete assessment of treatment benefit. Content validity measures the extent to which PROs evaluate the concepts most significant and relevant to a patient's condition and treatment [1,2]. Both the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have provided guidelines for development and validation of PROs consistent with good practice [3,4]. To be considered suitable for inclusion in labelling, PRO measure should be precise, sensitive to change and interpretable.

The St George's Respiratory Questionnaire (SGRQ) is a self-administered questionnaire that was developed to measure health status in patients with diseases of chronic airflow limitation [5–8]. It contains 50 items, and scores are calculated for a total score of respiratory health status and three domains: Symptoms (frequency and severity of respiratory symptoms), Activity (activities that cause or are limited by breathlessness) and Impacts (social functioning and psychological disturbances due to airway disease). Total and domain scores are calculated with all items weighted and are expressed as a percentage; higher scores indicate a worse state. The SGRQ was initially developed in patients with asthma [5–9] and evaluated in those with chronic obstructive pulmonary disease (COPD) [10]; it has since been validated in a range of conditions, including bronchiectasis [11], tuberculosis [12] and chronic pulmonary aspergillosis [13]. It is most commonly used as a measure of health status in COPD. The SGRQ has been used less frequently in patients with asthma but may be a valuable PRO for evaluation of severe asthma.

Essential characteristics of a PRO include demonstration of content validity and characteristics of quantitative validity, including reliability, construct validity, sensitivity to change and interpretability. To demonstrate reliability, the PRO should show evidence that it can measure items accurately. Scores should be consistent across items that measure a particular concept (internal consistency reliability) and should be consistent over time in patients with stable health (test-retest reliability). To demonstrate construct validity, the PRO must be shown to measure the concepts that it is intending to measure; PRO scores should be related to scores from other instruments measuring similar concepts (convergent validity) and relatively unrelated to scores from other instruments measuring unrelated concepts (discriminant validity). Scores should also differentiate between groups that are known or expected to differ with regard to the concept being evaluated (known-groups validity). The scores of a PRO must be sensitive to small changes if they are clinically meaningful, and it must be possible to interpret what constitutes a clinically important change (minimal important difference). Qualitative assessment also was conducted to identify the key symptoms and disease experience of severe asthma, to ascertain whether the SGRQ was relevant and comprehensive, to assess overall comprehension of the SGRQ, and to map the identified key aspects to concepts included in the SGRQ. The results of this assessment are reported elsewhere [14].

Not all PROs may be appropriate for all populations, so it is essential that a PRO is validated in all contexts and populations in which it will be administered. The SGRQ has been validated in a general asthma population, including patients with a broad range of asthma severities [9], but comprehensive evaluation in patients with severe asthma has not previously been reported. Thus, the primary objective of this post-hoc analysis of pooled data from two studies was to evaluate the structure, reliability, validity and responsiveness (sensitivity to change) of the SGRQ in patients with severe asthma.

2. Materials and methods

2.1. Study design

The analysis includes data from MENSA (NCT01691508) [15] and SIRIUS (NCT01691521) [16], two Phase III randomized, double-blind, placebo-controlled efficacy trials of mepolizumab. These post-hoc analyses of the SGRQ data from the MENSA and SIRIUS studies were guided by a pre-specified statistical analysis plan and conducted in the individual studies; in addition, a post-hoc analysis of pooled data from both studies was conducted. Unless otherwise stated, the results presented are from the pooled analysis; data from the individual analyses are provided as supplementary files (Tables S3–10).

Both studies recruited patients aged 12 years and older with severe eosinophilic asthma; although there were some differences in study design, they were considered sufficiently similar to allow pooling of data for the purpose of the assessment of psychometric properties of the SGRQ. Patients in MENSA were required to have a history of ≥2 asthma exacerbations treated with oral or systemic corticosteroids and regular treatment with high-dose inhaled corticosteroids (ICS) plus other controller(s), with or without maintenance oral corticosteroids (OCS). Patients in SIRIUS did not require a history of exacerbations, but did require high-dose ICS plus other controller(s) with the additional requirement of OCS (5–35 mg prednisone/day). In both trials, patients completed the SGRQ at Baseline (prior to first dose of mepolizumab) and at their Exit visit (MENSA Week 32; SIRIUS Week 24). Data at Exit were pooled from Week 32 of MENSA and Week 24 of SIRIUS, since treatment benefit was considered to have been achieved before study end, and these time points are sufficiently close to have little impact on the relationship between SGRQ and its comparator variables. Patients in SIRIUS received mepolizumab 100 mg subcutaneously (SC) or placebo every 4 weeks, whilst patients in MENSA received mepolizumab 100 mg SC, 75 mg intravenously (IV) or placebo every 4 weeks. The 100 mg SC and 75 mg IV doses are considered comparable based on bioavailability data [17]. Data were pooled across treatment groups; blinded data from all patients who completed at least the baseline assessment in MENSA and SIRIUS were included. Analyses were conducted on data from Baseline and Exit according to a predefined statistical analysis plan.

2.2. Item and scale characteristics

Distributional characteristics (N, mean, standard deviation [SD], range, median, ceiling and floor effects, and % missing) were used to assess item performance. The ceiling and floor effects reflect the inability of a measure to differentiate between patients located either at the most or least severe ends of the scale, respectively; i.e. they are all given either the best or the worst score. These items were defined in this study as >25% of patients selecting the most severe response (ceiling) and least severe response (floor).

Confirmatory factor analysis (CFA) applies structural equation modelling to evaluate the internal structure of a PRO. It considers the significance of the individual items (factor loadings) and the overall model fit. A factor loading of >0.40 is considered acceptable evidence that an item makes a significant contribution [18]. The overall model fit was assessed using three separate models: the comparative fit index (CFI) (values ≥ 0.9 indicate acceptable fit) [19]; the standardized root mean residual (SRMR) (values < 0.1 are considered acceptable) [20]; and the root mean square error of approximation (RMSEA) (values < 0.08 are considered acceptable) [21].