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Measurement properties and interpretation of three shortened versions of the asthma control questionnaire ☆

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Summary The Asthma Control Questionnaire (ACQ) measures the adequacy of asthma treatment as identified by international guidelines. It consists of seven items ($5 \times$ symptoms, rescue bronchodilator use and FEV_1% of predicted normal). A validation study suggested that in clinical studies measurement of FEV_1 and bronchodilator use may not be needed but this has never formally been tested in a clinical trial. The aims of this analysis were (1) to examine the measurement properties of three shortened versions of the ACQ (symptoms alone, symptoms plus FEV_1 and symptoms plus short-acting β_2-agonist) and (2) to determine whether using the shortened versions would alter the results of a clinical trial. In the randomised trial, 552 adults completed the ACQ at baseline and after 13 and 26 weeks of treatment. The analysis showed that the measurement properties of all four versions of the ACQ are very similar. Agreement between the original ACQ and the reduced versions was high (intraclass correlation coefficients: 0.94–0.99). Mean differences between the ACQ and the shortened versions were less than 0.04 (on the 7-point scale). Clinical trial results using the four versions were almost identical with the mean treatment difference ranging from -0.09 ($P = 0.17$), to -0.13 ($P = 0.07$). For interpretability, the minimal important difference for all four versions was close to 0.5. In conclusion, these three shortened versions of the ACQ can be used in large clinical trials without loss of validity or change in interpretation.

Introduction

The Asthma Control Questionnaire (ACQ)[1] was developed and validated to measure the primary

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clinical goal of asthma management as identified by international guidelines.[2–5] They indicate that to achieve good control, treatment should minimise day and night time symptoms, activity limitation, airway narrowing and rescue bronchodilator use and thus reduce the risk of life-threatening exacerbations and long-term morbidity. The importance of including all aspects of control in the assessment of individual patients was emphasised by a recent factor analysis which showed that clinical asthma is composed of distinct components which are not closely correlated with each other.[6] However, in some studies it may not be possible to collect airway calibre or short-acting β_2-agonists data. Previous analysis of non-clinical trial data suggested that when ACQ scores are analysed as group data, the heterogeneity of the way in which individual patients present with inadequate control is lost in the estimation of the mean and the need to measure each individual component of asthma control may become unnecessary.[7] In this analysis, ACQ data from a clinical trial was used to evaluate the measurement properties (reliability, responsiveness, validity and interpretability), of three shortened versions of the ACQ. In addition, we have examined whether the precision and accuracy of estimating the effect of the intervention on asthma control was maintained when the two questions concerning airway calibre and short-acting β_2-agonists use were omitted from the trial analysis.

Methods

Patients and study design

The analysis was conducted using the database from a 26-week, randomised, clinical study in which the combination of inhaled glucocorticosteroid plus long-acting, rapid-onset β_2-agonist was compared with the constituents taken separately. Of the 586 adults randomised, all of whom required inhaled steroids, 552 completed the ACQ and Mini Asthma Quality of Life Questionnaire (MiniAQLQ)[8] at baseline and after 13 and 26 weeks of treatment (Table 1). Complete details of the study are published elsewhere.[9]

Table 1 Demographics and baseline values.

Number of patients	552
Mean age (range) years	44.7 (18–81)
Gender M/F	249/303
Mean FEV_1% pred. (range)	87.9 (49.9–142.5)

Asthma Control Questionnaire

Ninety-one asthma clinicians, who were members of international asthma guideline committees,[2–5] participated in the development of the ACQ.[1] They identified the seven items in the questionnaires as being the most important for determining the adequacy of asthma control. Patients are asked to recall their experiences during the previous week and to respond to the first six questions (nighttime waking, symptoms on waking, activity limitation, shortness of breath, wheeze and rescue short-acting β_2-agonist use) on a 7-point scale (0=no impairment; 6=maximum impairment). Clinic staff score FEV_1% predicted pre-bronchodilator on a similar 7-point scale. The items are equally weighted and the ACQ score is the mean of the seven items and therefore between 0 (well controlled) and 6 (extremely poorly controlled). The ACQ has been validated and has strong measurement properties for use in both clinical practice and clinical trials.[1] In this analysis, three shortened versions of the ACQ (symptoms alone (questions 1–5), symptoms plus FEV_1 and symptoms plus short-acting β_2-agonist), were compared with the original ACQ.

Mini Asthma Quality of Life Questionnaire

The MiniAQLQ[8] consists of 15 questions in four domains (symptoms, activity limitations, emotional function and environmental stimuli) and measures the problems that adults with asthma find most troublesome in their day-to-day lives. Patients respond to each question on a 7-point scale from 7='not bothered at all' to 1='extremely bothered'. All questions are equally weighted and the overall score is the mean of the 15 responses. The MiniAQLQ has strong evaluative and discriminative measurement properties and the minimal important difference is 0.5 on the 7-point scale.[8]

Statistical analysis

Throughout the analysis, the original 7-item ACQ has been considered the gold standard (reference) against which the shortened versions have been compared (criterion validity). Data collected at baseline were used to determine differences (paired *t*-test), concordance (intraclass correlation coefficient) and internal consistency (Cronbach's alpha).

For all four instruments, test–retest reliability has been estimated as the within-subject standard deviation and related to the total standard

deviation as an intraclass correlation coefficient (ICC) using data from patients who remained stable (defined as having a change in MiniAQLQ score <0.5) between weeks 13 and 26. This statistic also provides evidence of the instrument's ability to discriminate between patients of different levels of impairment. Responsiveness (sensitivity to change) of the instruments was evaluated by comparing change scores between baseline and week 26 and by examining the clinical trial results. Both cross-sectional and longitudinal construct validity have been evaluated by comparing associations (Pearson correlation coefficient) with MiniAQLQ. For interpretability the change in ACQ scores that was equivalent to a change in MiniAQLQ score of 0.5 was calculated by regressing the change in ACQ scores on change in MiniAQLQ scores, using a geometric mean regression model.[10] This method allows for measurement errors in the independent (MiniAQLQ) variable as well as the dependent (ACQ) variable. The statistical package used was SAS version 8.2, SAS Institute Inc., Cary, NC 27513, USA.

Results

Criterion validity

At baseline the three shortened versions of the ACQ provided mean data that was very concordant with the original ACQ (ICC $\geqslant 0.94$) (Table 2). Although the 'symptoms alone' and 'symptoms plus β_2-agonist' versions were statistically different from the original ACQ, the actual differences were trivial ($\leqslant 0.04$ where the minimal important difference is approx. 0.5) and cannot be considered of clinical importance. Internal consistencies of the shortened versions were very similar to those of the original ACQ.

Reliability

Three hundred and eighty-one patients remained stable between weeks 13 and 26 and demonstrated reliability to be consistent and high (ICC $\geqslant 0.82$) for all four versions (Table 3).

Responsiveness

Change scores between baseline and 26 weeks for all four versions were all very similar (-0.48 to -0.52) (Table 2). However, the 'symptoms alone' and 'symptoms plus FEV_1' versions were statistically different from the original but the difference was trivial ($\leqslant 0.04$) and cannot be considered of clinical importance. The clinical trial analysis comparing change in asthma control between baseline and 26 weeks in the two treatment groups, showed very similar results for all four versions (Table 4). Taken in conjunction, these two analyses provide evidence that responsiveness (sensitivity to change) is very similar in the four versions.

Construct validity

Both cross-sectional and longitudinal correlations with the MiniAQLQ were very similar for all four versions (Table 5a and b). This evidence of construct validity, taken in conjunction with the criterion validity of the new versions (close concordance with the original), provides strong evidence that the new versions are measuring the same construct as the original ACQ.

Table 2 Shortened versions compared with the original ACQ (0=good control, 6=extremely poor control).

Instrument	Mean score at baseline mean (SD)	Difference between ACQ and short versions at baseline mean (SD) *P*-value*	Change score between baseline and 26 weeks mean (SD)	Difference between change in ACQ and change in short versions between baseline and 26 weeks mean (SD) *P*-value*	Concordance between ACQ and short versions at baseline ICC	Internal consistency at baseline Cronbach's alpha
All questions (ACQ)	1.52 (0.82)	n/a	−0.51 (0.76)	n/a	n/a	0.98
Symptoms alone	1.48 (0.93)	−0.039 (0.29) $p = 0.0015$	−0.48 (0.87)	0.027 (0.23) $p = 0.0072$	0.94	0.98
Symptoms plus FEV_1	1.52 (0.87)	0.004 (0.14) $p = 0.50$	−0.48 (0.789)	0.033 (0.13) $p < 0.0001$	0.99	0.97
Symptoms plus β_2-agonist	1.48 (0.86)	−0.037 (0.23) $p = 0.0002$	−0.52 (0.83)	−0.011 (0.16) $p = 0.12$	0.96	0.98

SD, standard deviation; ICC, intraclass correlation coefficient.
*Paired *t*-test.

Table 3 Reliability ($n = 381$).

Instrument	Within-subject SD	Between-subject SD	ICC
All questions (ACQ)	0.25	0.62	0.83
Symptoms alone	0.30	0.71	0.82
Symptoms plus FEV_1	0.26	0.65	0.84
Symptoms plus β_2-agonist	0.29	0.67	0.82

SD, standard deviation; ICC, intraclass correlation coefficient.

Table 4 Clinical trial results.

Instrument	Improvement on treatment A mean (SD)	Improvement on treatment B mean (SD)	Change on A–change on B *P*-value
All questions (ACQ)	−0.54 (0.68)	−0.45 (0.68)	−0.09 $p = 0.17$
Symptoms alone	−0.52 (0.78)	−0.40 (0.78)	−0.13 $p = 0.07$
Symptoms plus FEV_1	−0.51 (0.70)	−0.41 (0.70)	−0.10 $p = 0.11$
Symptoms plus β_2-agonist	0.55 (0.74)	−0.45 (0.74)	−0.10 $p = 0.13$

SD, standard deviation.

Table 5 Construct validity (Pearson correlation coefficients)

a) Cross-sectional (baseline)

Instrument	All questions (ACQ)	Symptoms alone	Symptoms + FEV_1	Symptoms + β_2-agonist
MiniAQLQ	0.72	0.77	0.72	0.76

b) Longitudinal (baseline - 26 weeks)

Instrument	Change in all questions (ACQ)	Change in symptoms alone	Change in symptoms + FEV_1	Change in symptoms + β_2-agonist
Change in MiniAQLQ	0.74	0.75	0.74	0.75

Interpretability

The minimal important difference for all four versions was close to 0.5. The geometric mean regression values and estimated standard errors were: All questions (ACQ): 0.46 (0.013); symptoms alone: 0.52 (0.015); symptoms+FEV_1: 0.46 (0.014) and symptoms+β_2-agonist: 0.49 (0.014).

Discussion

The results of this analysis provide strong evidence that when the FEV_1 and β_2-agonist questions are omitted from the original ACQ in clinical trials, the results generated will be very similar to those that would have been generated if the complete questionnaire had been used. The measurement

properties (reliability, responsiveness, internal consistency, construct validity and interpretability) of the three shortened versions of the ACQ are very similar to those of the original.

Although it is ideal to use the complete 7-item ACQ so that the individual components of clinical asthma may be examined separately, there are a number of situations in which it is not feasible to collect airway calibre or rescue short-acting β_2-agonist data. In epidemiological surveys, not only will some patients not have access to bronchodilators but there may be no means of measuring airway calibre. Although most pharmaceutical company trials are conducted in locations where both airway calibre and inhaled β_2-agonist use can be recorded, other non-pharmaceutical interventions (e.g. education, exercise) may have to be evaluated under less favourable conditions. In addition, phone, post and internet completion of the ACQ may have to be done without access to a home spirometer or peak flow meter.

The advent of a new rapid and long-acting inhaled β_2-agonist, formoterol, has given a new challenge to the assessment of asthma control. All the original guidelines were drawn up when only short-acting β_2-agonists were used as rescue medication.[2–5] However, recent studies with formoterol have shown that it can be used both as regular maintenance and a rescue intervention in patients already taking an inhaled steroid.[11,12] Therefore the optimum method for incorporating its use in the estimation of asthma control and also its scoring in the ACQ have not yet been established. This study has shown that this poses no problem for the assessment of asthma control in clinical trials of rapid and long-acting inhaled β_2-agonists because the bronchodilator question can be omitted.

We used a recognised 'anchor-based' method to estimate the minimal important difference of the ACQ. This is a clinical rather than statistical approach and links changes in the new instrument to clinically meaningful changes in a well-established instrument or changes in recognised health states.[13] Although not measuring the same constructs (concepts), the new and the established instruments are required to be fairly closely correlated so that regression models can be used. In this study, the correlation of $r = 0.74$ or higher between change in ACQ and change in MiniAQLQ allowed us to estimate the minimal important differences for the ACQ using the geometric mean model. A previous study which used a different anchor-based approach (global rating), showed that a single clinician estimated the minimal important difference for the ACQ to be 0.54.[14] With two different methods yielding similar results, we can be confident that the minimal important difference for the four versions of the ACQ is close to 0.5.

A recent factor analysis showed that clinical asthma has four distinct components: daytime symptoms plus daytime β_2-agonist use, nighttime symptoms plus nighttime β_2-agonist use, airway calibre and quality of life.[6] In other words, daytime β_2-agonist use correlates closely with daytime symptoms and nighttime use correlates closely with nighttime symptoms. This suggests that omission of β_2-agonist use may be less serious in the estimation of asthma control in individual patients than the omission of airway calibre which does not correlate well with either daytime or nighttime symptoms. However, until this has been investigated more thoroughly, clinicians looking after individual patients should endeavour to measure all the criteria identified in current guidelines[2–5,15] namely symptoms, activity limitations, airway calibre and rescue bronchodilator use.

In conclusion, this study has shown that the results and interpretation of clinical studies will not be affected if the questions concerning airway calibre and rescue bronchodilator use are omitted from the ACQ. However, these results only apply to group analyses and should not be applied to individual patients. Patients with poor perception of airway narrowing may have inadequately controlled asthma missed because they are asymptomatic and use no rescue bronchodilators. To minimise the risk of severe exacerbations in individual assessments, all components of asthma control should be measured.

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