

Editorial

Should asthma control be the guide for therapeutic decision-making?

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One of the challenges in studying asthma control is the lack of a gold standard definition. But acknowledging this limitation, Le Blanc et al. (1), in this month's edition of *Allergy*, have taken a major step forward in validating a quantitative scoring system for asthma control. The Global Initiative for Asthma (GINA)(2) has defined control with seven parameters that are consistent with goals of therapy. Four of these measures are patient centric (minimal symptoms, minimal exacerbations, low use of rescue bronchodilator and no limitations to physical activity), one is a physiological measure (PEF variability), one a measure of resource utilization (ED visit) and one a safety concern (no significant adverse events from treatment). No measure of inflammation is included in the current GINA definition of control. Although these goals are specifically articulated, the accurate assessment of the patient centric measures of asthma disease control may be limited by the accuracy of patient reporting and of physician recording of information. GINA explicitly recommends the use of a 'structured questionnaire' that can quantify patient symptoms over time.

Rabe et al. (3) have demonstrated that the goals of asthma management are not being achieved. In their study, over 50% of patients reported symptoms during the past 4 weeks for one or more of the following: asthma symptoms during the day, night or with exercise. Further 32–49% of patients with self-reported symptoms of severe persistent asthma stated that their asthma was well or completely controlled. These find-

ings were consistent throughout the world. The difficulty may be that patients do not perceive that the symptoms they are describing represent uncontrolled asthma and clinicians do not uniformly interpret and record these limitations illustrating the need for a structured reporting system.

Several excellent validated survey tools have been developed to assess patient report of control (4–6), but there is no comprehensive measure of asthma control. Spirometry or peak expiratory flow rate have been traditional standards of successful treatment especially in clinical trials. They are frequently designated as the primary endpoint. Although measures of lung function correlate well with symptoms and beta agonist use in some clinical trials, in others these two outcomes are disparate (7, 8). As examples, there are many patients with asthma, especially children and young adults of all disease severities, with normal spirometry and active symptoms (9). Second, there are patients with abnormal lung function consistent with obstructive airflow without significant report of symptoms (8). It is essential for these patients who fail to report symptoms that measures of lung function are performed. Finally, there are patients with a past history of asthma but no active symptoms, no recent medication use, normal lung function and yet evidence of active airway inflammation (10). The selection of any single parameter reduces the sensitivity of determining asthma that is not well controlled and may reduce the likelihood of appropriate intervention.

Boulet and associates developed the Asthma Control Scoring System (ACSS) with the recognition that asthma control requires a quantitative measure and not a 'binary decision' (11). They also acknowledge that in order to increase the predictive value of determining asthma control that an assessment should include clinical, physiological and inflammatory markers. Each of these determinants in the ACSS is equally weighted with 1–4 quantitative measures scored with a five-step scale. The present report in this month's *Allergy* further demonstrates the test–retest validity, the internal consistency, reproducibility, and the ability of the ACSS to reflect change in control over time (1). Furthermore, it establishes a correlation with the Asthma Control Questionnaire (6) and the Asthma Quality of Life Questionnaire (12).

Asthma control is a measurement of a point in time. It is a dynamic measure that reflects recent exposure to triggers as well as present therapy. But there is no consensus on either the timing or the frequency of measuring control. Intrinsic characteristics of asthma need to be accounted for in any measure of control. Diurnal variation in symptoms, pulmonary physiology and inflammation (13) may modify the assessment of control. Time of year alters the frequency and severity of symptoms (14). In the northern hemisphere if control is assessed in August and found to be excellent should controller medications be tapered knowing that the 'September epidemic' caused by rhinovirus occurs the next month? (15) What about the effect of seasonal pollens?

A large study of patients completing an asthma control survey demonstrated that improved control was associated with fewer exacerbations (16). Although evidence of disease activity demonstrated in any of the clinical, physiological or inflammatory parameters may indicate the need to increase the intervention, does the finding of a normal value over time in only one of these measures indicate that it is appropriate to reduce medications. These issues provide abundant areas for research.

Another important issue is the time interval between a change in therapy and reassessment of asthma control. This is dependent on the measure of interest and the intervention selection. Symptoms and lung function respond faster than bronchial hyper-reactivity and inflammation (17). If a patient's symptoms are improving and yet there is still evidence of active inflammation after 2–4 weeks of inhaled corticosteroids is that considered an adequate response and should treatment be maintained or altered? Furthermore, the choice of controller is an important variable. The time pattern of response as a variable is different for inhaled corticosteroids when compared with leukotriene receptor antagonists.

The term 'responder' is used to identify patient who improve with treatment. Improvement in the ACSS global score may provide an important method for assessing 'responders'. Depending on the effect size of

the response, improvement in one or more of the parameters may determine response. Therefore, a patient with better symptom report but without lung function improvement may still be considered a 'responder'. This is particularly important for the patient with a baseline normal FEV₁ and active symptoms. An intriguing clinical dilemma is how to categorize a patient who was assessed in August and found to have an ACSS score of 80 of 100, who is then infected with rhinovirus in September and has neither an increase nor decrease in their ACSS score. Is this patient benefiting from the therapy?

By including airway eosinophilia in the ACSS, LeBanc and associates are suggesting that markers of airway inflammation are important to consider. The papers by Sont (18) and Green (19) report that care directed by dynamic inflammatory markers may be improved over traditional symptom based management. The guidelines discuss in appropriate detail the importance of inflammation in asthma although the GINA measures of control do not include inflammation. The limitation of using sputum eosinophilia is illustrated in the present study (1) where one-third of patients did not produce sputum samples at baseline. In addition, not all facilities have the ability to perform this assay. Future studies may establish that alternative methods of assessment of inflammation such as exhaled nitric oxide may be more predictive and simpler to perform (20).

Embedded in the ACSS is a four-component quantitative measure of control that corresponds to the parameters of the three validated asthma control surveys (4–6). This section of the ACSS addresses the GINA criteria for a 'structured questionnaire'. The inclusion of spirometry may add to the sensitivity of determining asthma control (8). The importance of an assessment of inflammation is consistent with GINA and requires further validation studies to determine its impact on increasing the predictive value of determining control. Although the three components are possibly the most predictive, it is important to remember that good control starts with a simple survey tool (4–6) and then the sensitivity may be improved with each additional measure.

The ACSS is a major step forward in establishing a working definition of asthma control (1, 11). It becomes a potential standard against which other scoring systems can be assessed to determine whether an alternative system has an improved predictive value for asthma control. For patients, clinicians and researchers asthma control may be defined differently and yet if this is the goal of therapy there needs to be an accepted standard. LeBlanc and co-workers state that the need, at present, is to assess the utility of the ACSS as an instrument to improve asthma outcomes. Further reflection on the weight given to each parameters of control, the determination of the effect size for improved control and the frequency and timing of measures of control are all topics for further research.

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