The Seduction of Asthma Severity Categorization

Seduce: to lead away from accepted principles or proper conduct; to entice or beguile into a desired state

The American Heritage College Dictionary, 1997

In 1997, the National Heart, Lung, and Blood Institute published the seminal and comprehensive treatise "Expert Panel Report II: Guidelines for the Diagnosis and Management of Asthma.1" The fundamental principle guiding recommendations for asthma management in this handbook was a stepwise approach to pharmacotherapy based on a simple, clinically relevant, standardized method for classifying asthma severity. Adjusting the intensity of pharmacotherapy to the individual patient’s asthma severity seemed to be an intuitively reasonable principle, because it balanced the risks of side effects from more intensive pharmacotherapy (specifically higher doses of inhaled corticosteroids) against the potential benefits in more severe disease. There are three reasons, however, to be concerned that the method proposed in the Expert Panel Report II for classifying asthma severity is flawed. Practical observations suggest that clinicians cannot accurately use the asthma severity categorization method. The basic construct of the model is not supported by recent clinical observations. Severity categorization, as a concept, may not be as valuable as emphasizing asthma control and estimating the probability of certain poor outcomes. Given these concerns, the underlying principle of stepwise asthma pharmacotherapy based on severity categorization seems less appealing than initially suggested.

In this issue of CHEST (see page 2156), Baker and colleagues describe a relatively simple study of how pediatric asthma specialists categorize asthma severity based on the Expert Panel Report II method. Eight case summaries were mailed to board-certified pediatric allergists and pulmonologists, along with the Expert Panel Report II asthma severity categorization method. The specialists were asked to complete a multiple choice questionnaire that addressed asthma severity classification and treatment recommendations. There are some difficulties with the methods used in this study. Several of the cases described patients currently receiving treatment with controller medications. Although the authors make the cogent point that asthma specialists usually only see patients already receiving anti-inflammatory treatment, the Expert Panel Report II approach advocates severity categorization based on "clinical features before treatment." Unfortunately, agreement between the specialists and the "correct" asthma severity categorization, with appropriate explanation from the case summary, was not examined. Despite these weaknesses in the study design, it was obvious that there was poor agreement among the specialists in categorizing asthma severity. This observation should probably have been expected from previous work. Doerschug et al2 tested the content knowledge of residents, fellows, and faculty at the University of Iowa about the Expert Panel II report. In general, knowledge of these guidelines increased with advanced training, but overall was only moderate. Test performance in areas of estimating disease severity was especially disappointing; only 63% of the questions relating to asthma severity were answered correctly by asthma specialists. The results of these studies suggest that asthma specialists cannot reliably and accurately use the asthma severity categorization method proposed in the Expert Panel Report II.

The severity classification method divides patients into two major categories, either intermittent or persistent asthma. The distinction between these categories is based on clinical features and acts as a critical threshold for the introduction of long-term controller medications, specifically inhaled corticosteroids. Recent information suggests that using only clinical features to distinguish between intermittent and persistent asthma may not be reliable. Vignola and colleagues3 found evidence of airway inflammation on bronchial biopsy in 24 patients with mild, intermittent asthma. Van Den Toorn et al4 performed bronchial biopsies in 18 young patients with a history of atopic asthma, but who had been in clinical remission for at least 1 year. Clinical remission was defined as the complete absence of symptoms with no use of asthma medication. Despite clinical remission of asthma, the bronchial biopsies confirmed evidence of ongoing airway inflammation. There were elevated levels of major basic protein in the subepithelium and epithelium. Also detected were increased levels in the bronchial wall of interleukin-5, chymase, tryptase, and CD25+ cells. This information suggests that mild, intermittent asthma might not exist as a distinct entity if indexes of airway inflammation were considered.

Patients with persistent asthma are further categorized into mild, moderate, and severe categories. Limited information at present suggests that proper use of the Expert Panel Report II method will result in most patients being categorized as having severe persistent asthma. In a telephone survey of 1,788 randomly selected patients with asthma, symptom assessments resulted in 77.3% being categorized as having moderate/severe persistent asthma.5 However, patient recall during a telephone survey may not adequately capture symptoms over the previous weeks to months. A retrospective analysis of data
compiled during the performance of controlled clinical trials supporting the registration process for a new formulation of an inhaled corticosteroid was used to categorize asthma severity during the run-in phase of these trials prior to the initiation of randomized treatment. A strength of this analysis was that patients were required to complete a diary card twice daily describing symptoms and rescue medication use in these clinical trials, ensuring a rigorous approach to capturing symptoms. Of the 744 patients not receiving inhaled corticosteroids 508 patients (68.3%) were classified as having severe persistent asthma. If the Expert Panel Report II method results in the majority of patients with persistent asthma being categorized as severe, this subcategorization may provide only minimal incremental value.

The Expert Panel Report II method for asthma severity categorization relies on three equally weighted variables: daytime symptoms, nocturnal symptoms, and lung function. A scale has been constructed for each of these variables using clinically reasonable criteria to distinguish the different levels of severity. However, this approach is problematic in a disease in which there is often a dissociation between patient reported symptoms and objective evidence of airway obstruction. In the large retrospective analysis of patients entering clinical trials there was a poor correlation between symptoms and lung function. A disturbing observation in this analysis was that a single variable—nocturnal symptoms—most frequently determined categorization as severe, persistent asthma. Perhaps nocturnal symptoms are a more accurate guide to asthma severity than the other two variables. Alternatively, this observation may simply reflect that “frequent” nighttime symptoms may be too vague a criteria for a severe categorization. Other markers of disease activity, such as indexes of airway inflammation and bronchial hyperreactivity, were not included in this asthma severity categorization method. Sont et al tested, in a randomized, prospective study, whether regular measures of airway hyperresponsiveness by methacholine challenge testing would provide benefit in asthma management. They found that adjustment of inhaled corticosteroid doses based on both clinical variables and the results of the methacholine challenge tests resulted in more effective asthma control than using the clinical variables in the Expert Panel Report II alone. Another important clinical variable not included in the Expert Panel Report II method is a history of near-fatal asthma episodes. For many clinicians, a history of these severe attacks warrants consideration for long-term anti-inflammatory therapy even if symptoms were absent and lung function was normal. These observations suggest that a method for categorizing asthma severity based on symptoms and lung function may provide only limited value.

Asthma control and asthma severity are distinctly different concepts. Control means to hold in restraint or check. Asthma control relates to minimizing symptoms and rescue medication use. Symptoms and rescue medication use can be measured as a reflection of asthma control. Severe is defined as intense. If asthma is defined as an inflammatory airway disorder, asthma severity could be considered a reflection of the intensity of the intrinsic airway inflammation. Because the intensity of airway inflammation is not routinely measured in clinical practice, asthma severity has been defined indirectly by the minimal amount of inhaled corticosteroids required to achieve asthma control. The Expert Panel Report II method for asthma severity categorization actually provides little practical value, because in any individual patient, the balance of risks to benefits should be based on the doses of controller medications needed to successfully gain asthma control. If this approach were adopted, the clinician should also take into account the likelihood for such poor outcomes as a life-threatening asthma exacerbation and accelerated decline in lung function in adjusting the dose of controller medications.

Seduction is often based on superficial appearances. Asthma severity categorization seemed an attractive approach to the highly desired state of being able to balance the benefits and risks of pharmacotherapy in any individual with asthma. However, superficial appearances may have been deceiving. Limited information suggests that healthcare professionals cannot accurately use the currently recommended asthma severity categorization.
method. There are concerns that the method is flawed in its reliance on symptoms to distinguish intermittent from persistent asthma, its use of sub-categories of persistent asthma, and its dependence on a limited number of equally weighted clinical variables for overall categorization. An emphasis on asthma control, also considering the risks for certain poor outcomes, is conceptually more relevant than categorizing asthma severity in balancing the risks and benefits of asthma pharmacotherapy. It might be an appropriate time to reconsider the method for asthma severity categorization recommended in the Expert Panel Report II and its role in guiding pharmacotherapy.

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