Deep Inhalation Bronchodilation and Oral Corticosteroids in Asthma

Airway smooth-muscle hyperresponsiveness is a characteristic feature of asthma. Airway hyperresponsiveness is most commonly identified in the laboratory by the leftward shift of bronchoconstrictor (eg, methacholine) dose-response curves. A reduction in methacholine concentration producing a 20% fall in FEV₁ indicates increased ease of development of bronchoconstriction. Subjects with asthma also demonstrate an increased magnitude of bronchoconstriction, with progressive elevation of the level and eventual disappearance of the methacholine dose-response plateau. Another feature of the hyperresponsive airway smooth muscle in asthma is the bronchoactive effect of maximal lung inflation. In subjects with asthmatic airflow obstruction in the midst of an exacerbation, maximal inflation has a bronchoconstrictor effect. By contrast, in normal nonasthmatic subjects and subjects with mild asthma, maximal lung inflation has a potent bronchodilator effect.

While the mechanism(s) of airway hyperresponsiveness remain incompletely understood, there is little doubt that airway inflammation is linked to the hyperresponsiveness. Antiinflammatory therapy (eg, inhaled corticosteroid) can shift the methacholine dose-response curves to the right, can cause a reduction in the height of the dose-response plateau, and can restore or improve deep inhalation bronchodilation and bronchoprotection, at least at the mildly hyperresponsive end of the spectrum.

In this issue of CHEST (see page 58), Slats and colleagues used their established deep inhalation bronchodilation model to evaluate the effect of oral prednisone in a group of subjects with asthma who were stable and at least reasonably well controlled with inhaled corticosteroids. The primary end point was deep inhalation bronchodilation assessed by measuring flow at 40% vital capacity (V₄₀) from the maximal flow volume curve (M) compared to V₄₀ from the partial flow volume curve (P) and expressed as a ratio (M/P); a greater M/P ratio indicates more deep inhalation-induced bronchodilation. Following methacholine in a provocative concentration that reduced V₄₀ by 40% (PC₄₀), prednisone improved the magnitude of deep inhalation bronchodilation. Other surrogate measures of antiinflammatory effect were also improved by prednisone either within-group (airway responsiveness measured by FEV₁), or between prednisone and placebo groups (airway responsiveness measured by P and exhaled nitric oxide levels). This investigation demonstrates that deep inhalation bronchodilation, at least following methacholine-induced bronchoconstriction at the level of PC₄₀ flow volume curve, improves with more intensive antiinflammatory therapy and might be yet another surrogate measure to assess antiinflammatory efficacy. The important clinical message is that there is still room for improvement in subjects whose asthma is stable and acceptably controlled on inhaled corticosteroid.

The clinical applicability, however, of these data are not clear. This ties in to the important and as yet unanswered question as to what is the ideal or preferred method for monitoring asthma control. Guidelines recommend primarily symptoms (including morbidity and exacerbations) and spirometry. However, investigations such as that by Slats et al suggest additional benefits might be achieved by using additional measurements such as deep inhalation bronchodilation, airway responsiveness, exhaled nitric oxide, and others that were not evaluated in this study, such as indirect airway responsiveness, exhaled breath condensate, and the “gold standard” for airway inflammation, sputum eosinophils. As is frequently the case, a novel article such as this often raises as many questions as it answers, and further studies in this important area are necessary.

ACKNOWLEDGMENT: The author thanks Jacquie Bramley for assisting in the preparation of this editorial.

Donald W. Cockcroft, MD
Saskatoon, Canada

Dr. Cockcroft is Professor and Head of the Division of Respirology, Critical Care and Sleep Medicine, Royal University Hospital. The author has no financial disclosure to make on this topic. Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (www.chestjournal.org/misc/reprints.shtml).

Correspondence to: Donald W. Cockcroft, MD, FCCP, Division of Respirology, Critical Care and Sleep Medicine, Royal University Hospital, 103 Hospital Dr, Ellis Hall, 5th Floor, Saskatoon, SK S7N 0W8 Canada; e-mail: cockcroft@sask.usask.ca

DOI: 10.1378/chest.130.1.7

REFERENCES

8 Slats AM, Sont JK, van Klink RHCJ, et al. Improvement in bronchodilation following deep inspiration after a course of high-dose oral prednisone in asthma. Chest 2006; 130:58–65

Follow-up After an Asthma Hospitalization

Who Can Prevent Subsequent Exacerbations?

Asthma caused an average of 467,000 hospitalizations per year between 1995 and 2002.1 Most asthma hospitalizations are preceded by an emergency department visit (Emergency Medicine Network; unpublished data), and asthma accounts for a total of nearly 1.8 million emergency department visits per year.2 Although exact figures are not available, many of these emergency asthma visits are preventable. Since a prior asthma hospitalization or emergency department visit is the strongest risk factor for subsequent emergency hospital utilization,3 follow-up after an asthma hospitalization or emergency department visit presents a golden opportunity for tertiary prevention. However, there are substantial knowledge gaps regarding the type of follow-up that will significantly improve asthma outcomes.

Two randomized controlled studies4,5 have shown that achieving a primary care follow-up visit after an asthma emergency department visit can be facilitated but may not significantly improve asthma outcomes. Another nonrandomized controlled study6 also showed that reminder phone calls after an emergency department visit could increase primary care physician follow-up office visits, but this improved follow-up was not associated with a significant decrease in subsequent emergency hospital care or improved asthma control scores the next 12 months. In addition, a large survey7 of patients presenting to the emergency department with acute asthma showed that frequency of emergency department visits in the prior year was not related to having a primary care provider. This is not necessarily an indictment of primary care. Most patients who are followed up in primary care presumably do not require emergency hospital care. However, those who do require it apparently require something more than a return to primary care to significantly improve outcomes.

Several clinical trials have suggested that specialist follow-up may be more successful at preventing subsequent asthma hospitalizations than primary care follow-up. Mayo et al8 studied 104 adult asthmatic patients who had previously been admitted to the hospital due to asthma. Forty-seven patients were randomly assigned to an intensive outpatient treatment program in the chest clinic, and 57 patients continued to receive their previous outpatient care. Intervention patients required one third the number of hospital admissions per patient (p < 0.004) compared to usual-care patients. Hughes et al9 studied 95 children and adolescents who had been admitted with a diagnosis of asthma in the prior 5 years. Forty-seven intervention patients were randomized to follow-up by one pediatric respirologist, and 48 patients continued to receive regular care from their family physician or pediatrician. Intervention subjects had less school absenteeism than control subjects (mean, 10.7 vs 16.0 days, respectively; p = 0.04), but there were no significant differences in the rates of hospitalizations or emergency department visits during the study year. However, fewer days were spent in the hospital by the intervention patients compared to control patients (mean, 3.7 vs 11.2 days, respectively; p = 0.02).

Castro et al10 reported the results of a nurse specialist intervention program in asthmatic patients with a history of frequent health-care use. The intervention group consisted of 50 patients, and 46 patients who continued their usual care with their private primary care physician were assigned to the control group. There were 21 hospital readmissions for asthma in the intervention group compared to 42 readmissions for asthma in the control group (p = 0.04). Significant reductions in lost work or school days and

---


---

Downloaded from www.chestjournal.org at Walaeus Library on August 1, 2006