population in the salmeterol group compared with placebo. The risk was greater in the black subjects.

REVIEWER COMMENTS. This study was difficult to interpret, because the differentiation between respiratory-related versus asthma-related deaths was not clearly defined. The reasoning behind separating the analysis by study phase is also unclear. Health care providers should discuss the Food and Drug Administration’s long-acting β-agonist black-box warning (see www.fda.gov/cder/drug/infopage/LABA/default.htm) with patients and caregivers before and while on therapy. Primary care providers should consider specialty evaluation before starting long-acting β agonists to ascertain necessity. Additional studies are ongoing to assess the safety of combined products such as fluticasone/salmeterol and mometasone/formoterol. Long-acting β agonists should not be used as first-line therapy for asthma treatment and should only be used in combination with ICSs.

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Montelukast Improves Regional Air-Trapping Due to Small Airways Obstruction in Asthma

PURPOSE OF THE STUDY. To assess the effects of montelukast on regional air-trapping, airway hyperresponsiveness, and small-airway physiology using quantitative image analysis with high-resolution computed tomography (HRCT).

STUDY POPULATION. Sixteen patients (7 women, 9 men) aged 18 to 65 with no use of inhaled corticosteroids for the past 2 months, a forced expiratory volume in 1 second (FEV₁) of >60% predicted, a provocation dose that causes a 20% decrease in FEV₁, and a clinical diagnosis of asthma.

METHODS. The study was designed as a randomized, double-blind, placebo-controlled crossover trial. Subjects received either montelukast 10 mg or a placebo given once daily in the evening for 4 weeks. The subjects then crossed over to the alternate treatment for 4 more weeks. Regional air-trapping was assessed by HRCT at residual volume before and after methacholine challenge and was performed at baseline and after each of the drug phases was complete. Other indices of hyper-responsiveness and physiology were measured as well.

RESULTS. Significantly less regional air-trapping was seen on the premethacholine images of patients treated with montelukast. However, no effect on increases in regional air-trapping was seen on the postmethacholine images in these same patients. There were no differences seen in global indices of small-airways physiology between montelukast and placebo. Montelukast resulted in improved quality-of-life scores.

CONCLUSIONS. Montelukast improved small-airways disease in asthmatic subjects, but this improvement can only be detected by HRCT, not by physiologic studies.

REVIEWER COMMENTS. Although montelukast improved distal airway function, it is noted that at baseline, the patients in the montelukast group showed a greater degree of air-trapping, and this difference cannot be excluded as having an effect on the findings. One question that this study raised is why montelukast’s beneficial effects are only measurable with HRCT and not by physiologic means. The authors alluded to the poor sensitivity of physiologic indices and their large degree of intrasubject test variability. They also refer to the inhomogeneous pattern of small-airway involvement and the greater reliability of computer-derived quantitative image analysis versus qualitative radiographic techniques. Sample size was also limited in this study, which involved only mildly asthmatic subjects, indicating that further and expanded studies need to be performed. Montelukast’s inability to reduce hyperresponsiveness to methacholine should also be investigated further.

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Lack of Tolerance to the Protective Effect of Montelukast in Exercise-Induced Bronchoconstriction in Children

PURPOSE OF THE STUDY. To evaluate montelukast’s ability to inhibit exercise-induced bronchoconstriction in children at various time points over a treatment period of 28 days.

STUDY POPULATION. Thirty-two children, ranging in age from 6 to 12 years, with mild-to-moderate asthma.

METHODS. This study was designed as a multicenter, double-blind, randomized, parallel-group, placebo-controlled study. Subjects received either montelukast 5 mg or a placebo given once daily in the evening for 4 weeks. Exercise challenge and a pulmonary-function test were performed at baseline and then again at days 3, 7, and 28.

RESULTS. Montelukast provided significantly more protection against exercise-induced bronchoconstriction than placebo at each time point after treatment began. In addition, there was no significant difference in the percentage decrease of forced expiratory volume in 1 second for each drug at each of the days measured.
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