(FP) on the vascular component of airway remodeling among asthmatic patients.

**Study Population.** Thirty nonsmoking patients with mild/moderate asthma and baseline forced expiratory volume in 1 second values of ≥70% of predicted values. All patients had experienced no asthma attacks in the previous 2 months and controlled their symptoms with inhaled salbutamol only. Patients did not receive corticosteroids in the 6 months before the study and had not experienced any respiratory infections for 4 weeks before the investigation.

**Methods.** This was a double-blind, randomized, parallel-group study, with patients receiving FP at either 500 or 100 μg twice daily, with a spacer device. Treatments were administered for 6 weeks, and patients were assessed in the clinic on 5 separate days. Symptom diaries were maintained, spirometry and methacholine challenges were performed, and fiber-optic bronchoscopies were undertaken at specific time points during the investigation. Healthy volunteers underwent bronchoscopies for comparison.

**Results.** Eighteen of 30 patients completed the study protocol, and adequate paired biopsy material for immunostaining was obtained for 16 patients, 8 in the group that received 500 μg of FP twice daily and 8 in the group that received 100 μg of FP twice daily. At baseline, patients with asthma differed significantly from the healthy volunteers with respect to the number of vessels and the vascular area. Among the asthmatic patients, the number of vessels was correlated with vascular area (P < .01) and the number of mast cells (P < .01). Bronchial responsiveness to methacholine, asthma symptom scores, and numbers of inflammatory cells decreased significantly after both low- and high-dose FP (P < .05); however, basement membrane thickness decreased only after high-dose FP (P < .05).

**Conclusions.** The results from this investigation demonstrated that, among patients with mild/moderate asthma, a high dose of inhaled FP, administered for 6 weeks, could significantly affect airway remodeling by reducing both submucosal vascularity and basement membrane thickness.

**Reviewer’s Comments.** The authors claim that this is the first published evidence that short-term treatment with high-dose FP significantly reduced the vascular component of airway remodeling among patients with mild/moderate asthma. The small number of subjects who completed the investigation and the short time of medication administration seem to limit the overall conclusions regarding the effects of high-dose FP on airway remodeling. These data could have significant clinical implications for the use of higher doses of inhaled corticosteroids in the ongoing treatment of patients with mild/moderate asthma, who might be receiving lower doses of these medications to control their disease.

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**LEUKOTRIENE ANTAGONIST THERAPY**

**A RANDOMIZED, CONTROLLED TRIAL OF INTRAVENOUS MONTELUKAST IN ACUTE ASTHMA**


**Purpose of the Study.** To determine whether the addition of intravenously administered montelukast to standard therapy for patients with acute asthma would cause rapid improvement in airflow obstruction, as well as improvement in clinically relevant outcomes such as hospitalization or prolonged or additional antiasthma therapy.

**Study Population.** Patients, 15 to 54 years of age, who were presenting with acute asthma were screened for enrollment. Requirements included a history of asthma for ≥1 year, a history of tobacco use of <10 pack-years, and no concomitant therapy with systemic corticosteroids, leukotriene modifiers, anticholinergic agents, or long-acting β-agonist bronchodilators.

**Methods.** This was a multicenter, double-blind, randomized, placebo-controlled, parallel-group study with a screening period and an active study period. Two doses of intravenously administered montelukast (7 and 14 mg) or matching placebo were evaluated. Serial spirometric assessments were performed at 10, 20, 40, 60, and 120 minutes and 3 and 6 hours after intravenous study drug infusion.

**Results.** A total of 201 patients were randomized, and complete data were available for analysis for 194. During the screening period, there was no difference in forced expiratory volume in 1 second responses between the 7-mg and 14-mg montelukast groups. Montelukast improved forced expiratory volume in 1 second values in the first 20 minutes after intravenous administration (mean percentage change from prerandomization baseline value: 14.8% and 38.6% for the pooled montelukast and placebo treatment groups, respectively; P = .007). This benefit was observed at 10 minutes and for 2 hours after intravenous therapy. Patients treated with montelukast tended to receive less β-agonist and to experience fewer treatment failures, compared with patients receiving placebo. The study drug and placebo were similarly tolerated, and no unexpected adverse effects were observed.

**Conclusions.** Intravenously administered montelukast, in addition to standard therapy, provided rapid benefits and was well tolerated among patients with acute asthma.

**Reviewer’s Comments.** A substantial proportion of asthma exacerbations continue to require prolonged management in an emergency department setting or hospitalization. In addition to standard asthma therapies, interventions involving inhaled ipratropium, intravenously administered magnesium, and inhaled helium/oxygen mixtures have been investigated. Intravenously administered montelukast, as an adjunctive therapy for these patients, may provide added benefits with current treatment options. These results must be confirmed and, in future studies, montelukast use among pediatric patients <15 years of age should be investigated.

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**EFFECTS OF MONTELUKAST AND BECLOMETHASONE ON AIRWAY FUNCTION AND ASTHMA CONTROL**


**Purpose of the Study.** The primary objective of asthma therapy is the maintenance of asthma control, and the most common measures of such control in clinical studies reflect pulmonary function; forced expiratory volume in 1 second (FEV1) is often used. The authors sought to use a different parameter, ie, days of asthma control, as the primary measure, because observations regarding the need for both rescue medications and unscheduled asthma-related health care are central to perceived wellness.

**Study Population.** This multicenter study involved 782 individuals, ≥15 years of age, with a ≥1-year history of moderate persistent asthma (baseline FEV1: 50–85% of predicted values) but no controller therapy at the time of...
enrollment. All patients were required to have a current daily need for inhaled albuterol and documented airway reversibility of ≥15% at the time of entry.

Methods. Patients were randomly assigned to receive montelukast (10 mg, each evening), beclomethasone (200 μg, twice daily), or placebo, with a ratio of 3:3:1. The use of spacers was not required. Compliance was monitored with pill counts and simple patient reports of inhaler use. A day of asthma control was defined as a day with no more than 2 puffs of albuterol treatment, no nocturnal awakenings with asthma, and no need for acute medical attention. An asthma exacerbation was defined as ≥3 consecutive days without asthma control. An occurrence of sustained asthma control was defined as ≥3 consecutive days with control. Subjects completed diary cards during the 2-week, single-blind, run-in period and during the 6-week, double-blind, treatment phase. The primary measure was the percentage of days of asthma control during the treatment phase. Secondary measures included average daily albuterol use, percentages of patients with and without attacks, asthma exacerbations, occurrence of sustained asthma control, rescue corticosteroid use, and changes in FEV₁ from baseline values. Clinic visits occurred every 3 weeks during the double-blind phase, and spirometry was performed at that time.

Results. The mean percentages of days of asthma control for patients who received montelukast or beclomethasone were similar and were significantly better than that for placebo recipients. Both drugs resulted in significant improvements in FEV₁, but the benefit was greater with beclomethasone. There was no difference between the active treatment groups in any of the other secondary measures, and both treatments were clearly superior to placebo for most parameters.

Conclusions. Montelukast and beclomethasone were of similar efficacy, as judged by indices of clinical control other than FEV₁. The latter parameter may underestimate clinical effectiveness.

Reviewer’s Comments. Considering the severity of asthma among these individuals, it might seem surprising that these drugs performed so similarly during the 6-week active treatment phase. One might be tempted to attribute this to presumed poor compliance with the inhaled corticosteroid, compared with the convenient montelukast tablet, especially because beclomethasone monitoring was through reports alone. However, there is no doubt that beclomethasone outperformed the leukotriene receptor antagonist in FEV₁ measures, suggesting reasonable compliance and greater potency in improving pulmonary function. Six weeks is probably too short a period to detect differences in major attacks between the 2 treatment groups, and it is likely that a much longer treatment period would have revealed more favorable results for most parameters, including the primary measure, for the inhaled corticosteroid-treated group. Almost by definition, most of these patients had asthma that was too severe to be treated with just 1 drug; a more interesting comparison would have been among patients with mild persistent disease, without histories of hospitalization or recurrent acute attacks.

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MONTELUKAST IMPROVES ASTHMA CONTROL IN ASTHMATIC CHILDREN MAINTAINED ON INHALED CORTICOSTEROIDS


Purpose of the Study. To evaluate whether montelukast as adjunctive therapy improves asthma control and whether montelukast has corticosteroid-sparing effects among children treated with low or moderate inhaled corticosteroid (ICS) doses.

Study Population. Thirty-six children, 6 to 14 years of age, with mild/moderate persistent asthma who were being maintained with a stable low or moderate dose of ICS were randomly assigned to receive montelukast or matching placebo.

Methods. After a single-blind, run-in period of 2 weeks for assessment of incomplete control of asthma symptoms (period I), qualified subjects were randomized in a double-blind, placebo-controlled, 2-period, parallel-group study designed to investigate the effects of montelukast as 4-week adjunctive therapy (period II) and to investigate its effects on the ability to taper the dose of ICS during a 20-week period (period III). Subjects maintained daily asthma diaries, and spirometry was performed monthly.

Results. In period II, both the mean number of β₂-agonist rescue-free days per week and the difference in the number of rescue-free days were significantly greater for the montelukast-treated subjects, compared with the placebo-treated subjects (6 days vs 3.18 days, P = .0002; 4.47 days vs 0.05 days, P = .0001; respectively). In period III, the percentage changes in ICS doses were not statistically significantly different between the montelukast and control groups (P = .10), but subjects receiving montelukast experienced an average 17% reduction in ICS dose, compared with a 64% increase in ICS dose among subjects receiving placebo. Also, although the findings were not statistically different, 32% of subjects receiving montelukast were weaned completely off the ICS, compared with 18% in the placebo group.

Conclusion. Montelukast significantly increased the number of rescue-free days among symptomatic children with mild/moderate persistent asthma.

Reviewer’s Comments. Although this was a pilot study with a small patient population, the results are encouraging for those who care for children with asthma, as well as for parents, who are often concerned about the use of corticosteroid medications. Additional studies with a larger population of patients with mild/moderate asthma and a group of patients with severe asthma are warranted.

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ANTI-IgE THERAPY

EVALUATION OF LONG-TERM SAFETY OF THE ANTI-IMMUNOGLOBULIN E ANTIBODY, OMALIZUMAB, IN CHILDREN WITH ALLERGIC ASTHMA


Purpose of the Study. To evaluate safety parameters for 1-year treatment with omalizumab among children 5 to 12 years of age.

Study Population. A total of 225 patients, 5 to 12 years of age, with a mean duration of asthma of 6.1 years (range: 1–12 years) were studied. All patients had allergic asthma, which had been well controlled for ≥3 months before the study with inhaled corticosteroid doses equivalent to 168
EFFECTS OF MONTELUKAST AND BECLOMETHASONE ON AIRWAY FUNCTION AND ASTHMA CONTROL

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