and the number of nighttime awakenings; and fewer courses of oral steroids per year. The average daily dose of ICS received per patient was lower in the 2 B/F groups. All of the medications were well tolerated. Pediatric subjects receiving B/F demonstrated greater linear growth than those on higher-dose budesonide.

CONCLUSIONS. Use of B/F for both maintenance and rescue is associated with a lower asthma-exacerbation rate and an improvement in several other indicators of asthma control. In addition, subjects using B/F in this manner have a decreased exposure to oral steroids and require less use of rescue medication. The authors suggest that the timing of the increase in ICS use for asthma exacerbations, rather than the total ICS dose administered, provides the greater improvement in efficacy.

REVIEWER COMMENTS. The rapid onset of action of the β2-agonist formoterol suggests that it could be used as a rescue medication, although this is not a licensed indication. Use of the B/F combination as a controller and rescue presents an attractive option because of the decrease in asthma morbidity compared with either B/F and SABA or ICS and SABA. Even with the use of B/F for rescue, the mean dose of ICS received was lower than in the ICS-and-SABA group (240 vs 640 μg/day in the adults) and only slightly higher than in the B/F-and-SABA group (240 vs 160 μg/day in the adults). This combination product is not yet licensed in the United States, but if approved, B/F used in this fashion will offer a novel treatment alternative for asthmatic patients. In addition, B/F maintenance and rescue therapy may provide a significant benefit for patients for whom adherence to 2 separate drugs may present serious difficulties or confusion.

URL: www.pediatrics.org/cgi/doi/10.1542/peds.2006-0900SSS

Ivan N. Chinn, MD
Mary Dell Railey, MD
Larry W. Williams, MD
Durham, NC

Characterization of Within-Subject Responses to Fluticasone and Montelukast in Childhood Asthma

PURPOSE OF THE STUDY. Asthmatic individuals vary in their responses to inhaled corticosteroids (ICSs) and leukotriene antagonists (LTRAs). The authors of this study sought to determine if responses are concordant for both types of drugs and sought markers for responses.

STUDY POPULATION. Children (aged 6–17 years) with mild-to-moderate asthma. They had asthma symptoms or bronchodilator use on average at least 3 days/week over the preceding 4 weeks and improvement in forced expiratory volume in 1 second (FEV1) of ≥12% after maximal bronchodilation or methacholine PC20 (provocative concentration causing a 20% decrease in FEV1) of ≤12.5 mg/mL. Children with severe asthma were excluded, as were those with recent use of corticosteroid or LTRA.

METHODS. After a 5- to 10-day characterization phase, participants were randomly assigned to 1 of 2 crossover treatment sequences with 8-week periods of either active ICS (fluticasone 100 μg twice daily) or an age-appropriate dose of montelukast. During the active-treatment period for one drug, the participant received a placebo for the alternative drug. Baseline-only characterization included various asthma biomarkers. The primary outcome measure was percentage change in prebronchodilator FEV1 from baseline to the end of the treatment period. “Response” was defined as improvement in FEV1 of at least 7.5%.

RESULTS. Fifty-five percent of the 126 participants showed no response to either drug, whereas 23% responded to fluticasone alone, 17% responded to both, and 5% responded to montelukast alone. Compared with those who responded to neither drug, those who responded to fluticasone alone had higher exhaled nitric oxide, serum immunoglobulin E, serum eosinophilic cationic protein, and total eosinophil count, along with lower methacholine PC20 and lower pulmonary function. Favorable response to montelukast alone was associated with younger age and shorter disease duration. Greater differential response to fluticasone over montelukast was associated with higher bronchodilator use and response, along with higher exhaled nitric oxide and serum eosinophilic cationic protein levels and lower methacholine PC20 and pulmonary function.

CONCLUSIONS. Responses to fluticasone and montelukast vary. Children with low pulmonary function or high levels of biomarkers should start with ICSs. In children with less severe disease, it would be reasonable to start with either ICSs or LTRAs. Asthma therapy might soon move from the current approach, which is based on mean responses in populations, to one predicated on a given person’s asthma phenotype and genotype.

REVIEWER COMMENTS. The vast majority of asthmatic patients in a primary care practice can maintain excellent control with one or the other of the above-mentioned drugs as simple monotherapy. History is paramount in assessing asthma severity, especially because the above-described biomarkers are largely unavailable to the pediatrician. It is tantalizing to consider a time when we will be able to more accurately target successful treatment in advance.
Comparative Efficacy and Safety of Low-Dose Fluticasone Propionate and Montelukast in Children With Persistent Asthma


PURPOSE OF THE STUDY. To evaluate efficacy, safety, health outcomes, and cost-effectiveness of fluticasone propionate (FP) versus montelukast in children with asthma

STUDY POPULATION. Children aged 6 to 12 years with persistent asthma.

METHODS. Multicenter, randomized, double-blind, double-dummy, parallel-group study of 342 children with persistent asthma. Children received either FP 50 μg twice daily via Diskus or montelukast 5 mg once daily for 12 weeks. The primary efficacy variable was percent change in morning predose forced expiratory volume in 1 second at the end point.

RESULTS. Compared with montelukast, children treated with FP experienced a significantly greater increase in mean percent forced expiratory volume in 1 second, mean morning peak expiratory flow rate, and mean evening peak expiratory flow rate. Children treated with FP also experienced significantly greater reductions in total supplemental albuterol use, mean nighttime albuterol use, and mean nighttime symptom scores compared with children treated with montelukast. There were no significant differences between the groups for daytime asthma symptom scores, daytime albuterol use, percent symptom-free days, or adverse events. Parent and physician satisfaction ratings were significantly higher for FP treatment. The daily total asthma-related cost per patient in the FP group was approximately one third of the cost in the montelukast group.

CONCLUSIONS. FP was significantly more effective than montelukast in improving pulmonary function, asthma symptoms, and rescue albuterol use. Both therapies had similar safety profiles.

Montelukast, Compared With Fluticasone, for Control of Asthma Among 6- to 14-Year-Old Patients With Mild Asthma: The Mosaic Study


PURPOSE OF THE STUDY. Per current asthma guidelines, montelukast is considered a suitable alternative to inhaled corticosteroids (ICSs) for the treatment of mild persistent asthma, and this study was conducted to evaluate the use of oral montelukast compared with inhaled fluticasone in children with mild asthma.

STUDY POPULATION. Children (aged 6–14 years) with mild persistent asthma participating in the Montelukast Study of Asthma in Children (MOSAIC) study.

METHODS. In this 12-month, multicenter, randomized, double-blind, noninferiority comparison study, patients were randomly assigned to receive oral montelukast 5 mg once a day (n = 495) or inhaled fluticasone 100 μg twice a day (n = 499) after an appropriate run-in period. After baseline evaluations, patients were evaluated at 4-month intervals with spirometry and review of an asthma diary card. The primary end point, the percentage of asthma rescue-free days (RFDs), included days with no rescue-medication use and no asthma-related primary care or urgent care visits or hospitalizations. Secondary end points included forced expiratory volume in 1 second (FEV₁), use of additional asthma medications, asthma attacks, β-agonist use, and peripheral blood eosinophil levels.

RESULTS. The mean percentage of RFDs was 84% in the montelukast group compared with 86.7% in the fluticasone group. The least-squares means difference was 2.8% (95% confidence interval: −4.7% to −0.9%), which represents a difference of <1 day/month. Both montelukast and fluticasone were associated with improvement in FEV₁ (percent predicted) from baseline as well as reduction in the percentage of days with β-agonist use, reduction in blood eosinophils, and improvement in patient-perceived asthma control and asthma quality-of-life scores; however, fluticasone was significantly favored in terms of FEV₁, β-agonist use, asthma control, and quality of life. Montelukast was associated with the increased use of systemic corticosteroids (17.8% vs 10.5%; P = .001) and a higher percentage of patients with an asthma attack (32.2% vs 25.6%) compared with fluticasone.
Characterization of Within-Subject Responses to Fluticasone and Montelukast in Childhood Asthma

James R. Banks and Timothy Andrews

*Pediatrics* 2006;118:S43

DOI: 10.1542/peds.2006-0900TTT

Updated Information & Services

including high resolution figures, can be found at:
/content/118/Supplement_1/S43

Permissions & Licensing

Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
/site/misc/Permissions.xhtml

Reprints

Information about ordering reprints can be found online:
/site/misc/reprints.xhtml
Characterization of Within-Subject Responses to Fluticasone and Montelukast in Childhood Asthma
James R. Banks and Timothy Andrews
Pediatrics 2006;118:S43
DOI: 10.1542/peds.2006-0900TTT

The online version of this article, along with updated information and services, is located on the World Wide Web at:
/content/118/Supplement_1/S43