Montelukast as Add-on Therapy to β-Agonists and Late Airway Response

PURPOSE OF THE STUDY. To evaluate montelukast’s ability to inhibit the late-phase airway response after allergen exposure in adults with house dust mite–induced asthma.

STUDY POPULATION. Thirty-five adults (19 men, 16 women) aged 18 to 31 with mild, stable asthma and sensitivity to house dust mites were included.

METHODS. This study was designed as a randomized, double-blind, single-dose, placebo-controlled, crossover trial. Subjects underwent serum testing for antigen-specific immunoglobulin E (IgE) to house dust mite. Sensitized subjects were then examined for airway infections and underwent spirometry and determination of their fraction of nitric oxide in exhaled air (FeNO). They were then challenged with increasing concentrations of inhaled Dermatophagoides farinae via a nebulizer system. Testing was stopped when the patient’s forced expiratory volume in 1 second (FEV₁) decreased at least 20% (early airway response [EAR]), they experienced significant clinical symptoms, or they received a cumulative dose of 1270 mg. Patients were then given 1 puff of salbutamol (0.1 mg) and either montelukast (10 mg) or a placebo. FEV₁ was measured for the following 8 hours with a decrease of at least 20% demonstrating a late airway response (LAR). Formoterol (12 µg) was then given to treat those patients. Subjects returned at least 2 weeks later and were crossed-over into the other group.

RESULTS. Of the 35 subjects in the study, 12 showed no significant EAR on 1 or both study days, 11 showed only an EAR, and 12 demonstrated both an EAR and LAR. This last group was analyzed further. The difference in FEV₁ from baseline values 3 to 8 hours after challenge was expressed as the area under the FEV₁ time-response curve (FEV₁-AUC). The FEV₁-AUC of patients on placebo was $-2.47 \pm 1.32$ vs $-0.768 \pm 1.68$ for the patients on montelukast ($P < .005$). Subjects with a dual response had a significantly higher baseline FeNO than those with no response ($56.4$ vs $21.0$ ppb; $P < .05$).

CONCLUSIONS. Montelukast was able to block the late-phase airway response in subjects who responded dually to the allergen challenge. In addition, patients with a higher baseline FeNO seemed more likely to develop an LAR than those with lower ones.

Attenuation of the September Epidemic of Asthma Exacerbations in Children: A Randomized, Controlled Trial of Montelukast Added to Usual Therapy

PURPOSE OF THE STUDY. To evaluate whether montelukast, when added to usual asthma therapy, would affect the asthma symptoms experienced during the annual asthma epidemic occurring each year when school resumes after summer vacation.

STUDY POPULATION. Participants included 194 subjects from 2 to 14 years of age with physician-diagnosed asthma. More than 90% of the children had prescriptions for an inhaled corticosteroid (ICS).

METHODS. Children were randomly assigned to receive either an age-appropriate dose of montelukast ($n = 98$) or...
placebo (n = 96). The first tablet was taken the evening of September 1 and continued nightly for 45 days. Asthma symptoms, cold symptoms, use of oral prednisone, and unscheduled physician visits resulting from asthma were recorded daily. Subjects were instructed to take the tablet in addition to their usual asthma therapy.

RESULTS. Children who received montelukast experienced 53% fewer days with “worse asthma symptoms” compared with children who received placebo (3.9% vs 8.3%; P < .02). In addition, there was a 78% reduction in the number of unscheduled visits to a physician for asthma (4 vs 18; P = .011). These improvements were seen in patients with and without cold symptoms. Among boys, the greatest benefit from montelukast was seen in those aged 2 to 5 years. Girls benefited most from montelukast when they were between the ages of 10 and 14 years.

CONCLUSIONS. Montelukast, when added to usual asthma therapy, reduced the risk of worsening asthma symptoms and unscheduled physician visits during the annual September asthma epidemic.

REVIEWER COMMENTS. It has long been recognized that epidemics of asthma exacerbations occur annually after students return to school after summer vacation. This study demonstrates that montelukast, a leukotriene-receptor antagonist, could be used in conjunction with usual asthma medications to attenuate some of these annual symptoms. The study population enrolled in this study was composed largely of persistently asthmatic children, based on the fact that >90% were prescribed ICSs. Additional studies are needed to investigate whether a similar reduction in asthma symptoms would be seen in subjects with less-severe asthma. In addition, compliance with the use of prescribed ICSs in this study was relatively poor, with only 47% of subjects using an ICS routinely. This is in agreement with other studies that have shown that ICS prescription filling is at its lowest just before the return to school. It remains to be seen whether simply improving compliance with prescribed ICSs at the start of the academic school year would also lead to a significant reduction in asthma symptoms.

Comparative Study of Budesonide Inhalation Suspension and Montelukast in Young Children With Mild Persistent Asthma


PURPOSE OF THE STUDY. To evaluate the efficacy of budesonide inhalation suspension (Pulmicort respules) compared with montelukast (Singulair) for controlling asthma symptoms in young children with mild persistent asthma.

STUDY POPULATION. This was a prospective study of 395 children, aged 2 to 8 years, diagnosed with mild persistent asthma recruited from 55 US centers. Approximately 12% of the subjects had previous histories of inhaled corticosteroid (ICS) use.

METHODS. Subjects were randomly assigned to receive either budesonide 0.5 mg or montelukast 4 to 5 mg daily and were followed for 52 weeks. Compliance was assessed by daily electronic diary review. For mild asthma exacerbations, step-up therapy consisted of the addition of a morning dose of budesonide 0.5 mg in both arms. For severe asthma exacerbations, subjects received a 3- to 10-day standardized course of oral steroids. The primary end point was evaluated by using the intention-to-treat population and was defined as time to first additional medication for asthma worsening at 52 weeks. Secondary end points included the time to additional asthma medication and rates of occurrence of mild and severe asthma exacerbations. Changes in symptom scores, peak flows, rescue-medication use, and pulmonary-function test results were also evaluated.

RESULTS. Kaplan-Meier probability curves showed that the primary outcome measurement, time to the first additional asthma medication, was not significantly different between the 2 groups at 52 weeks (P = .3). There was a significant increase in the time to first additional asthma medication in the budesonide group compared with the montelukast group at 12 weeks (P = .05). The percentage of subjects requiring step-up therapy in the budesonide group versus the montelukast group at 12 weeks was 29.1% versus 38.6% (not significant [NS]), at 26 weeks was 41.3% versus 48.2% (NS), and at 52 weeks was 52% versus 56.9% (NS), respectively. The budesonide group achieved significantly improved morning and evening peak flow values compared with the montelukast group at 12 weeks (P = .005–.007). The rate of mild and severe asthma exacerbations per subject per year in the budesonide and montelukast groups was 1.23 and 1.63, respectively (P = .034). There was no significant difference in the number of severe asthma exacerbations between the 2 groups. Both treatment groups showed nonsignificant improvements in changes from baseline asthma scores, 24-hour rescue-medication use, and medication- and asthma-free days.

CONCLUSIONS. Both budesonide and montelukast are effective and well-tolerated as controller medications in children aged 2 to 8 years with mild persistent asthma. Results favored budesonide for several secondary outcome measures.
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