

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 ICS 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.

URL: www.pediatrics.org/cgi/doi/10.1542/peds.2008-2139XXX

Christine Virnig, MD
James E. Gern, MD
Madison, WI

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

Szeffler SJ, Baker JW, Uryniak T, Goldman M, Silkoff PE. *J Allergy Clin Immunol.* 2007;120(5):1043-1050

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.

REVIEWER COMMENTS. Previous studies have shown that ICSs are more effective asthma-controller medications compared with montelukast in children older than 6 years. Although this study failed to show statistical significance in the primary outcome, it provides data supporting certain treatment benefits of ICSs in children younger than 6 years (257 of 395 children were <5 years old). Compared with previous studies, these children had milder asthma, with only 12% having taken ICSs before enrollment.

URL: www.pediatrics.org/cgi/doi/10.1542/peds.2008-2139YYY

Julia Wisniewski, MD
Anna Nowak-Wegrzyn, MD
New York, NY

Effect of Different Antiasthmatic Treatments on Exercise-Induced Bronchoconstriction in Children With Asthma

Stelmach I, Grzelewski T, Majak P, Jerzynska J, Stelmach W, Kuna P. *J Allergy Clin Immunol*. 2008;121(2):383–389

PURPOSE OF THE STUDY. To compare the effectiveness of different patterns of antiasthmatic treatments to protect children from exercise-induced bronchospasm (EIB).

STUDY POPULATION. This was a randomized, double-blind, placebo-controlled study of 100 children aged 6 to 18 years with atopic asthma sensitive only to house dust mites and EIB. Subjects must have had a resting forced expiratory volume in 1 second (FEV₁) of $\geq 70\%$ predicted and at least a 20% drop in FEV₁ after exercise to qualify for the study.

METHODS. Participants were randomly assigned to a 4-week double-blind, placebo-controlled trial to receive 1 of the following treatments: (1) budesonide 100 μg + formoterol 4.5 μg twice daily; (2) budesonide 100 μg twice daily + montelukast 5 or 10 mg at bedtime; (3) montelukast 5 or 10 mg at bedtime; (4) budesonide 100 μg twice daily; or (5) placebo alone. All study arms had matching placebo medications from which active drugs were omitted (eg, group 1 had placebo tablets in place of montelukast, etc). At randomization and after 4 weeks on the study medication(s), a treadmill exercise test was performed to evaluate the effectiveness of treatment.

RESULTS. Ninety-one subjects with a median age of 11.3 to 12.2 among the groups completed the study. Preexercise FEV₁ and EIB, as represented by the area under the curve of time-response curve and by maximum percentage decrease in FEV₁ after exercise, did not differ at baseline between the groups. EIB was diminished with all treatments when compared with placebo. The effect of treatment with budesonide plus montelukast and with montelukast alone were greater than budesonide

alone or budesonide plus formoterol ($P < .001$). The budesonide-plus-formoterol group was also better than budesonide alone, but these results did not reach significance ($P = .59$).

CONCLUSIONS. Budesonide plus montelukast or montelukast alone were the most effective treatments for EIB in children.

REVIEWER COMMENTS. This was the first study in asthmatic children that evaluated both monotherapy and combination therapy for the reduction of EIB. This study highlights the importance of controller therapy in childhood asthma and the effects on EIB between therapeutic options recommended for childhood asthma. In particular, consideration for the use of montelukast as monotherapy or in combination therapy with inhaled corticosteroids is indicated for EIB in children with similar asthmatic phenotypes.

URL: www.pediatrics.org/cgi/doi/10.1542/peds.2008-2139ZZZ

Joshua L. Kennedy, MD
Stacie M. Jones, MD
Little Rock, AR

Adverse Effects of Inhaled Corticosteroids in Funded and Nonfunded Studies

Nieto A, Mazon A, Pamies R, et al. *Arch Intern Med*. 2007;167(19):2047–2053

PURPOSE OF THE STUDY. Evidence regarding the safety profile of drugs may vary depending on study sponsorship. The authors aimed to evaluate differences between studies funded by the pharmaceutical manufacturer of the drug (PF) and those with no pharmaceutical funding (NoPF) regarding the finding and interpretation of adverse effects of inhaled corticosteroids.

METHODS. The authors assessed the safety reporting of inhaled corticosteroids in 275 PF and 229 NoPF studies identified by a Medline search using prespecified criteria.

RESULTS. Overall, the finding of statistically significant differences for adverse effects was significantly less frequent in PF (34.5%) than in NoPF (65.1%) studies (prevalence ratio [PR]: 0.53 [95% confidence interval (CI): 0.44–0.64]). This association became nonsignificant (PR: 0.94 [95% CI: 0.77–1.15]) after controlling for design features (such as dose or use of parallel groups) that tended to be associated with less-frequent findings of adverse effects and were more common in PF studies. Among studies that found a statistically significant increase in adverse effects associated with the study drug, the authors of PF articles concluded that the drug was “safe” more frequently than the authors of NoPF studies (PR: 3.68 [95% CI: 2.14–6.33]).

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

Julia Wisniewski and Anna Nowak-Wegrzyn

Pediatrics 2008;122;S219

DOI: 10.1542/peds.2008-2139YYY

Updated Information & Services

including high resolution figures, can be found at:
http://pediatrics.aappublications.org/content/122/Supplement_4/S219

Subspecialty Collections

This article, along with others on similar topics, appears in the following collection(s):

Therapeutics

http://www.aappublications.org/cgi/collection/therapeutics_sub

Allergy/Immunology

http://www.aappublications.org/cgi/collection/allergy:immunology_sub

Asthma

http://www.aappublications.org/cgi/collection/asthma_sub

Permissions & Licensing

Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:

<http://www.aappublications.org/site/misc/Permissions.xhtml>

Reprints

Information about ordering reprints can be found online:

<http://www.aappublications.org/site/misc/reprints.xhtml>

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN®



PEDIATRICS[®]

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

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

Julia Wisniewski and Anna Nowak-Wegrzyn

Pediatrics 2008;122;S219

DOI: 10.1542/peds.2008-2139YYY

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

http://pediatrics.aappublications.org/content/122/Supplement_4/S219

Pediatrics is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. Pediatrics is owned, published, and trademarked by the American Academy of Pediatrics, 345 Park Avenue, Itasca, Illinois, 60143. Copyright © 2008 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 1073-0397.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN[®]

