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Patterns of Quick-Relief and Long-term Controller Medication Use in Pediatric Asthma

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study. The final ICS dose for fluticasone was 370 $\mu\text{g}/\text{day}$ (95% confidence interval [CI]: 263–477 μg) in the FeNO group and 641 $\mu\text{g}/\text{day}$ (95% CI: 526–756 μg ; $P = .003$) in the guideline group. The rate of exacerbations per patient per year was 0.49 (95% CI: 0.31–1.49) in the FeNO group, compared with 0.9 (95% CI: 0.31–1.49; $P = .27$) in the guideline group. There was no difference in the number, frequency, or time of first exacerbation between groups. There was no significant difference in nighttime awakenings, bronchodilator use, percent symptom-free days, or number of oral corticosteroid courses. There also was no difference in percent sputum eosinophils or pulmonary-function tests.

CONCLUSIONS. With the use of FeNO, control of asthma can be obtained with a lower ICS dose.

REVIEWER COMMENTS. The values for FeNO differ from other studies because a flow rate of 250 mL/second was used instead of 50 mL/second. The control group had downward titration of dose on the basis of symptoms, which was achieved only in a minority of patients. This may have magnified the observed difference in the ICS dose. This and subsequent studies suggest that markers of airway inflammation are becoming accepted as important surrogate markers of asthma control.

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The Prevalence of Ibuprofen-Sensitive Asthma in Children: A Randomized Controlled Bronchoprovocation Challenge Study

Debley JS, Carter ER, Gibson RL, Rosenfeld M, Redding GJ. *J Pediatr.* 2005;147:233–238

PURPOSE OF THE STUDY. To determine the prevalence of ibuprofen-sensitive asthma in school-aged children with mild or moderate persistent asthma.

STUDY POPULATION. Children ($n = 100$) between the ages of 6 and 18 years with a 2-year history of asthma.

METHODS. Ibuprofen (10 mg/kg) was administered via a randomized, double-blind, placebo-controlled crossover trial. At 0.5, 1, 2, and 4 hours postingestion, spirometry and physical examinations were performed. Children taking leukotriene receptor antagonists or with a known sensitivity to aspirin or ibuprofen sensitivity were excluded.

RESULTS. Two subjects (2%) had bronchospasm after administration of ibuprofen, with decreases in the forced expiratory volume in 1 second (FEV_1) of 35% and 25%, respectively. The maximal drop in FEV_1 occurred 1 hour after ibuprofen administration in both subjects. Clinical manifestations of shortness of breath and wheezing on

auscultation were noted in both patients. Resolution of symptoms and pulmonary-function values occurred after administration of albuterol. Neither patient had a decrease in FEV_1 after placebo. Neither patient had a history of ibuprofen use before study enrollment. Two additional patients had a decrease in FEV_1 of 15% (with no change after placebo) but remained asymptomatic with normal physical examinations.

CONCLUSIONS. In this study of children ages 6 to 18 years with mild or moderate persistent asthma, the prevalence of ibuprofen-induced bronchospasm was 2%. This is much lower than previous estimates (9%–28%) of aspirin-sensitive asthma in children.

REVIEWER COMMENTS. Use of inhaled corticosteroids by 70% of study subjects and exclusion of patients with severe asthma and those using leukotriene receptor antagonists may have resulted in an underestimate of the prevalence of ibuprofen-sensitive asthma. However, given the widespread use of ibuprofen as an over-the-counter analgesic and antipyretic, pediatricians should be aware of the possibility of ibuprofen-induced asthma exacerbations.

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Patterns of Quick-Relief and Long-term Controller Medication Use in Pediatric Asthma

Walders N, Kopel SJ, Koinis-Mitchell D, McQuaid EL. *J Pediatr.* 2005;146:177–182

PURPOSE OF THE STUDY. To simultaneously examine adherence to long-term controller and quick-relief medications and to contrast patterns of medication use in children with asthma.

STUDY POPULATION. There were 75 children aged 8 to 16 years diagnosed with persistent asthma and prescribed quick-relief and long-term medications by metered-dose inhaler. Participants were a subsample of a larger adherence study.

METHODS. This was a cross-sectional, 1-month follow-up study. The primary outcome measure was adherence to both medications as measured by electronic monitoring devices. A classification framework for contrasting adherence patterns between medication classes was developed to identify cases for individual analysis.

RESULTS. High levels of nonadherence to long-term controller medications (median: 46% of prescribed doses taken) and variable patterns of quick-relief medication use (range: 0–251 doses over the month) were documented, but consistent relationships between patterns of medication use across both classes were not found. Individual cases identified by the classification scheme il-

lustrated the complexity and clinical utility of contrasting adherence patterns.

CONCLUSIONS. Monitoring long-term controller medication adherence may be more predictive of morbidity than quick-relief medication use except in outlier cases, in which monitoring both medication types may be valuable for clinical and empirical purposes.

REVIEWER COMMENTS. Medication adherence has long been identified as a key factor in overall asthma outcome. For example, self-reporting quick-relief and long-term controller medication use, canister weighing, pharmacy records, and electronic monitoring have all been used to assess medication adherence. Of these methods, electronic monitoring, which is the most costly and technologically complex, is generally accepted as the most accurate method for monitoring adherence. Inadequate daily medication adherence has been widely documented in patients with asthma and has been linked to morbidity and increased health care costs. Although it was not surprising that nonadherence to long-term controller medications was common in this investigation, it was very interesting that no statistically significant relationship was found between adherence with quick-relief and long-term controller medication classes. For example, the investigators' hypothesis that quick-relief and long-term controller medication use would demonstrate an inverse relationship (eg, higher long-term controller medication use corresponding to lower reliance on quick-relief medications) was not confirmed. The investigators suggest that novel strategies to enhance appropriate medication use, such as better tracking the use of long-term controller medications and providing feedback regarding actual use, may be effective in improving adherence in asthma patients.

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Asthma as a Risk Factor for Invasive Pneumococcal Disease

Talbot TR, Hartert TV, Mitchel E, et al. *N Engl J Med*. 2005;352:2082–2090

PURPOSE OF THE STUDY. To determine if asthma is a risk factor for invasive pneumococcal disease.

STUDY POPULATION. Patients 2 to 49 years of age in a Tennessee Medicaid program (TennCare) with >1 year of continuous enrollment during the study period (1995–2002). For each patient with invasive pneumococcal disease, 10 age-matched controls were chosen. A total of 11 counties in Tennessee with a population of 2.8 million participated in the study. Asthma was defined as ≥ 1 inpatient diagnoses (admission or emergency depart-

ment visit), ≥ 2 outpatient diagnoses, or use of asthma-related medications. High-risk asthma was defined as an admission for asthma, an emergency department visit, long-term use of oral steroid, or use of ≥ 3 short-acting β agonists per year.

METHODS. Invasive pneumococcal disease was defined as isolation of strep pneumonia from a normally sterile site (eg, blood, cerebrospinal fluid, pleural fluid, surgical aspirate, joint fluid, and/or bone). The organisms were serotyped.

RESULTS. A total of 635 patients with invasive pneumococcal disease and 6350 controls were identified. A total of 18% (114 patients) with asthma had an invasive infection compared with 8.1% (516 patients) in the control group. Patients with asthma had increased risk of invasive disease (odds ratio: 2.4; 95% confidence interval: 1.9–3.1). In patients with high-risk asthma, the annual risk for invasive disease was 4.2 of 10 000 compared with 2.3 of 10 000 in the low-risk asthma group and 1.2 of 10 000 in the control group.

CONCLUSIONS. Asthma is an independent risk factor for invasive pneumococcal disease.

REVIEWER COMMENTS. The risk of invasive disease did not depend on comorbid conditions or advancing age. This is the first study to show the association and, if upheld with further data, will significantly affect our recommended immunization strategy for patients with asthma.

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Exercise-Induced Dyspnea in Children and Adolescents: If Not Asthma Then What?

Abu-Hasan M, Tannous B, Weinberger M. *Ann Allergy Asthma Immunol*. 2005;94:366–371

PURPOSE OF THE STUDY. Exercise-induced asthma (EIA) is the most commonly recognized cause of exercise-induced dyspnea (EID) in children and adolescents. However, EID in otherwise healthy children and adolescents may have other causes besides asthma. The purpose of this study is to report the outcome of evaluations for EID when other signs and symptoms of asthma were absent or there was no response to previous use of an inhaled β_2 agonist.

STUDY POPULATION. One hundred forty-two patients, 6 to 21 years old (mean: 14 years), with EID were studied.

METHODS. In this retrospective study, investigators reviewed the results of all exercise tests performed in otherwise healthy patients with EID between 1996 and 2003. Physiologic measures assessed included preexer-

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