POEMs

Patient-Oriented Evidence that Matters

Each month, the POEMs editorial team reviews more than 90 journals of interest to primary care physicians, identifying articles you need to know about to stay up to date. We call these articles POEMs (Patient-Oriented Evidence that Matters) because they address common primary care problems, report outcomes that matter to patients, and, if valid, require us to change the way we practice. The 8 most important articles are critically appraised here each month. Occasionally, we include articles that confirm an important practice for which there had been only weak evidence previously (POEs – Patient-Oriented Evidence) or research that is focused on intermediate outcomes (DOEs – Disease-Oriented Evidence). We call attention to the latter so improper changes in currently valid practices are prevented. The collected reviews are available online at www.jfampract.com. Additional POEMs and other important evidence-based material are published in a monthly newsletter called *Evidence-Based Practice* (available through subscription—phone: 1-201-782-5726; fax: 1-201-391-2778).

Combined Oral and Inhaled Steroids for Acute Asthma

Rowe BH, Bota GW, Fabris L, Therrien SA, Milner RA, Jacono J. Inhaled budesonide in addition to oral corticosteroids to prevent asthma relapse following discharge from the emergency department: a randomized controlled trial. JAMA 1999; 281:2119-26.

Clinical question **Does the combination of inhaled and oral steroids reduce the risk of relapse in patients with acute asthma?**

Background Patients with acute asthma exacerbations often require an evaluation in an emergency department (ED). A course of an oral corticosteroid is frequently prescribed at discharge and has been shown effective in preventing relapse. Inhaled corticosteroids in the acute setting are prescribed less often, and their effectiveness has been less well established. This study examined whether inhaled corticosteroids confer any additional benefit in preventing asthma relapse when added to oral corticosteroids.

Population studied The study population initially included a total of 1006 patients with acute asthma exacerbations presenting to a community teaching ED in a mid-sized Canadian city. After exclusions, 263 patients were eligible for enrollment. Approximately 30% refused to participate, leaving 188 subjects. Patients entered the study after receiving standard ED asthma treatment. Patients aged 16 to 60 years with pretreatment peak expiratory flow rate (PEFR) <80% of the predicted rate were included. Exclusion criteria included complicated comorbidity (eg, cardiovascular or renal disease or HIV infection) and the use of oral or inhaled steroids within a week before the study.

Study design and validity This was a double-blinded placebo-controlled randomized clinical trial. After standard asthma treatment, patients were discharged and given oral prednisone (50 mg/d) for 7 days. Additionally, they were randomized to receive either placebo or budesonide dry powder inhaler (800 µg twice a day) for 21 days. In the budesonide and placebo groups, respectively, mean age was 26 and 29 years, 46% and 48% were current smokers, 54% and 55% had no regular physician, 81% and 86% were taking β_2-agonists at the initiation of the study, and initial PEFR was 45% and 54% of the predicted rate.

Outcomes measured The primary outcome measured was asthma relapse rate, defined as an unscheduled visit for worsening asthma symptoms within 21 days of enrollment. The authors did not provide details regarding severity or outcomes of reported relapses. Other outcomes measured included quality of life and patients' global assessment of asthma severity (on a validated questionnaire), use of β_2-agonist inhaler, pulmonary function data, and asthma symptoms.

Results During the 21-day period, relapse rates were 12.8% for the budesonide group and 24.5% for the placebo group (P <.05; relative reduction in relapse = 48%; number needed to treat = 9). There was also a statistically significant improvement in quality of life and a decrease in β_2-agonist inhaler use, asthma symptoms, and global assessment of asthma in the budesonide group. There was no significant difference in PEFR or hospital admission rate at 21 days. Five patients in the budesonide group and 3 in the placebo group either dropped out of the study or were lost to follow-up. Compliance was better than 90% for both the 7-day course of oral prednisone and the 21-day inhaled medication regimen. Interestingly, there was a statistically significant increase in hoarseness and sore throat experienced by the control group, indicating that perhaps the placebo was not completely inert.

Recommendations for clinical practice **Adding high-dose inhaled budesonide to oral prednisone in selected patients (those not already using inhaled steroids who were discharged from the ED following standard treatment for asthma exacerbations) reduced the rate of unscheduled return visits for worsening symptoms. Budesonide use did not, however, affect the overall low rate of hospitalization. The addition of inhaled budesonide also improved symptoms, quality of life, and frequency**

of β_2-agonist use. These effects may not pertain to other high-dose inhaled steroids, as the authors cite an abstract that showed no benefit in pulmonary function from flunisolide in a similar study. Using the current average wholesale price for the budesonide Turbuhaler, the cost to prevent one office or ED visit would be approximately $1000. This would imply a fairly high cost-to-benefit ratio; formal cost-benefit analysis is yet to be done.

Maura Hamrick, PhD, MD
M. Lee Chambliss MD, MSPH
Moses Cone Family Medicine Residency
Greensboro, North Carolina
E-mail: lee.chambliss@mosescone.com

Which Inhaled Corticosteroid for Asthma?

Raphael GD, Lanier RQ, Baker J, Edwards L, Rickard K, Lincourt WR. A comparison of multiple doses of fluticasone propionate and beclomethasone dipropionate in subjects with persistent asthma. J Allergy Clin Immunol 1999; 103:796-803.

Clinical question **Which inhaled steroid — fluticasone (Flovent) or beclomethasone (Beclovent, Vanceril) — is more effective for treating persistent asthma?**

Background The National Institutes of Health's treatment guidelines for persistent asthma recommend the use of inhaled corticosteroids. Although the guidelines recognize categories of inhaled steroids and provide guidance for the use of low, medium, and high dosages, none is recommended.

Population studied A total of 399 nonsmoking men and women aged 12 years and older with chronic asthma requiring daily inhaled steroids for at least 6 months were enrolled. Each person had taken 8 to 12 puffs per day of either beclomethasone or triamcinalone for at least 1 month before enrollment. Screening and baseline forced expiratory volume in 1 second (FEV_1) values were between 45% and 80% of predicted normal. Subjects had reversible lung function (≥12% increase in FEV_1 after 2 puffs of albuterol). Continuation of theophylline or salmeterol was allowed if taken at stable and approved doses and if the morning dose was withheld before all study visits. The only other permitted asthma medication was the albuterol metered-dose inhaler (Ventolin) for symptomatic relief. Exclusion criteria included the use of oral or intravenous steroids, leukotriene modifiers, or nedocromil sodium for 1 month before the study.

Study design and validity This randomized double-blind double-dummy parallel-group clinical trial was conducted at 23 specialty asthma and primary care study centers and occurred over 12 weeks. There were 4 treatment groups: low-dose fluticasone (44 µg/puff, 2 puffs twice daily); medium-dose fluticasone (110 µg/puff, 2 puffs twice daily); low-dose beclomethasone (42 µg/puff, 4 puffs twice daily); and medium-dose beclomethasone (42 µg/puff, 8 puffs twice daily).

Before the 12-week randomization, there was a 2-week single-blind run-in period. During this phase, subjects took beclomethasone (42 µg/puff, 4 puffs twice daily) with a placebo instead of their usual inhaled steroid. Eligibility for the study was evaluated, compliance with medication use was assessed, and a baseline was established.

Spirometry was done at screening (before the run-in period), at baseline (after the run-in period), and after 1, 2, 4, 6, 8, 10, and 12 weeks. Subjects kept diary cards documenting supplemental albuterol use, morning and evening peak expiratory flow rates (PEFRs), night awakenings caused by asthma, and asthma symptoms on a scale of 0 to 3 (where 0 = none and 3 = severe).

This well-designed study with 4 demographically similar treatment groups took great care to ensure compliance and similar knowable patient baselines using the run-in phase. Spacers were not used and 8 puffs twice daily of 42 µg/puff beclomethasone was used instead of 4 puffs twice daily of the 84 µg/puff product.

Outcomes measured Outcomes measured included FEV_1, daily albuterol use, asthma symptoms, PEFRs, and nighttime awakenings due to asthma.

Results Fluticasone at both the low and medium dose improved FEV_1 by 0.31 L (14%) and 0.36 L (15%), respectively, compared with improvements of 0.18 L (8%) and 0.21 L (9%) with the low and medium doses of beclomethasone. In each outcome category, with the exception of night awakenings, fluticasone bested beclomethasone: morning PEFR (P <.001), evening PEFR (P = .06), puffs per day of albuterol (P = .004), percent days without albuterol use (P = .01), asthma symptom scores on a 0 to 3 scale (P = .024), and percent days without symptoms (P = .027). Overall, greater improvements in pulmonary function parameters occurred with fluticasone treatment (P <.034). Similar side effect and withdrawal rates were reported between the various groups.

Recommendations for clinical practice **When treating persistent asthma, fluticasone is more effective than beclomethasone in equivalent doses. This is true for both disease-oriented outcomes (eg, spirometry) and for patient-oriented outcomes (eg, fewer asthma attacks). Fewer attacks means less rescue albuterol, which translates into lower patient expense. Flovent requires**