

Study Population. Subjects were asthmatic children aged 6 to 18 years who had no other chronic illness. There were 347 children assigned to the vaccine group and 349 assigned to the placebo group.

Methods. The primary outcome was the number of asthma exacerbations associated with virologically proven influenza infection. Study subjects and their families scored daily symptoms in a diary, and when symptoms reached a predefined level, a pharyngeal swab for influenza was taken. The symptom diary was maintained from the day after administration of inactivated influenza vaccine or placebo on approximately November 1 until April 1 of the following year. Secondary outcomes included the duration and severity of the asthma exacerbations, adverse effects of vaccination, and the number, duration, and severity of all asthma exacerbations. Influenza virus–specific antibody titers were measured before vaccination, 14 to 21 days afterward, and at the end of the influenza season.

Results. In each group, 344 participants provided diary data for the primary outcome. The groups were generally similar in baseline characteristics, with almost 90% of children having used maintenance medication for asthma in the previous 12 months. There were 486 reports of symptom scores that met the predefined criteria for an asthma exacerbation (vaccine group: 251; placebo group: 235), with 42 of the resultant throat swabs testing positive for influenza (vaccine group: 24; placebo group: 18). The difference in the number of asthma exacerbations was not significant (95% confidence interval: 34% reduction to 161% increase). There were no significant differences found between the 2 groups for any of the secondary outcomes measured. Antibody levels 14 to 21 days after vaccination were increased only in the vaccine group. However, when comparing the 14- to 21-day titers to those at the end of the season, ~23% of subjects in the placebo group and 10% in the vaccine group had a fourfold increase in influenza-specific titers.

Conclusions. The authors concluded that influenza vaccination was not more effective than placebo in reducing the number of asthma exacerbations caused by influenza infections in children.

Reviewers’ Comments. Current guidelines that recommend the use of influenza vaccination in asthmatics are based on epidemiologic evidence. A recent Cochrane review on influenza vaccination in asthmatics found insufficient evidence to make conclusions about the risks or benefits of influenza vaccination, primarily because of a lack of randomized trials. Although this study was a randomized trial, the low attack rate of influenza (~6% of subjects tested positive by pharyngeal swab) makes it difficult to draw conclusions from the results. The study’s sample size was calculated based on the assumption of a 30% influenza attack rate, leaving it significantly underpowered to detect an effect at such a low attack rate. If the question of efficacy of influenza vaccine in reducing asthma morbidity is ever to be answered convincingly, a large randomized trial, probably over several influenza seasons, will be needed.

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RHINITIS THERAPY AND THE PREVENTION OF HOSPITAL CARE FOR ASTHMA: A CASE-CONTROL STUDY


Purpose of the Study. To examine the effect of treatment of allergic rhinitis on hospitalization and emergency department visits in patients with concomitant allergic rhinitis and asthma.

Study Population. Three hundred sixty-one subjects and 1444 control patients with allergic rhinitis and asthma who were at least 6 years of age.

Methods. A case-control analysis of patients with asthma and concomitant allergic rhinitis was performed between 1996 and 1997 in a large managed care organization in northeastern United States. Diagnosis, procedure, laboratory, health care utilization, and pharmacy records were analyzed to determine if treatment of allergic rhinitis affected the frequency of asthma exacerbations. Patients fulfilled the requirements for diagnosis of asthma and allergic rhinitis within a 12-month period. Patients were defined as asthmatic if they had ≥2 claims with diagnostic codes for asthma; had claims with 1 asthma diagnosis code and 1 asthma-related prescription; or filled 2 asthma-related prescriptions. Patients with allergic rhinitis had ≥2 claims with allergic rhinitis diagnosis codes; ≥2 prescriptions for second-generation antihistamine; ≥2 prescriptions for nasal corticosteroids; 1 prescription for a second-generation antihistamine and 1 prescription for a nasal corticosteroid; or a claim with 1 allergic rhinitis diagnosis code and at least 1 prescription for a second-generation antihistamine and a nasal corticosteroid.

Results. Treatment of allergic rhinitis was associated with a lower frequency of emergency department visits and hospitalization resulting from asthma. Patients receiving monotherapy with a nasal corticosteroid had significantly lower risk of emergency department visits (odds ratio [OR]: 0.75) and hospitalization (OR: 0.56). A similar trend was seen with treatment with a second-generation antihistamine alone. Treatment with a combination of nasal corticosteroids and second-generation antihistamines was associated with additional lower risk of emergency department visits (OR: 0.37) and hospitalization (OR: 0.22).

Conclusions. Treatment of allergic rhinitis lowers the risk of asthma-related health care utilization in patients with concomitant allergic rhinitis and asthma.

Reviewer’s Comments. This was a useful study in that it supports the National Heart, Lung, and Blood Institute guidelines for long-term successful management of patients with asthma and concomitant allergic rhinitis. This is the first large case-control study to definitively show a positive relationship between treatment of allergic rhinitis and lowered risk for asthma health care utilization. Findings support the idea of “one airway,” and physicians should remain cognizant of the benefits of treating the upper airway in patients with lower-airway disease.

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HOW DO PATIENTS DETERMINE THAT THEIR METERED-DOSE INHALER IS EMPTY?

Rubin BK, Durotøy L. Chest. 2004;126:1134–1137

Purpose of the Study. To evaluate how patients determine that their metered-dose inhalers (MDIs) are empty and to measure doses available of MDIs in different laboratory conditions.

Study Population. Fifty consecutive patients attending a pediatric asthma center at Wake Forest University (Winston-Salem, NC).

Methods. Fifty new pediatric patients and their caregivers who used MDIs regularly were asked the question “How do you know when it is time to replace your inhaler?” and then were asked to elaborate on their answers.
For the second part of the study, samples of MDIs (Flovent, Serevent, albuterol, and Qvar) were obtained from the manufacturers and studied in the laboratory. They evaluated the MDIs to determine how many actuations could be emitted and obtained weights during the process. They evaluated the usefulness of floating the MDIs in water to determine if they were full or empty, as has been suggested in the past for tracking the content of MDIs.

Results. The survey revealed that 72% of subjects determined that their MDI was empty when they could no longer hear a sound when actuated. Another 20% said they replaced it when it was “old” without giving specific details, although most said “within a month or so” or “after a while.” Four patients stated that they were told to float their MDI in water to determine if it was full (sinks to the bottom) or empty (floats), although none had actually done it. The majority (78%) said they knew they were supposed to shake the MDI before using it, but only half shook the MDI when their technique was evaluated later. In the laboratory, MDIs had similar flotation patterns, with mean flotation angles of 27.6 to 31.7° when empty. Water obstructed the valve or collected near the valve during this procedure 27% of the time. The chlorofluorocarbon inhalers (Flovent, Serevent, and albuterol) had a mean of 86% more audible puffs and Qvar 54% more than the stated manufacturer actuations. Shaking the MDI before actuation increased the doses available for the chlorofluorocarbon inhalers significantly.

Conclusions. Most patients studied did not know how to tell if their MDI was empty, and many did not shake the MDI before actuation, which can limit the amount of drug delivered. These results may in part explain the poor adherence with refills for MDIs, because patients may not realize that they are not receiving a full dose of active drug (because all of the MDIs studied had significantly more actuations than noted on the canister), which the authors termed “pseudo-adherence.” The only way to truly track the number of remaining doses in MDIs is to count each dose. Most MDIs will emit more drug doses if the device is shaken before actuation. Floating MDIs in water is not accurate for assessing remaining doses and often will clog the valve.

Reviewer’s Comments. This article demonstrates one of the limitations of MDIs in the inability of patients to accurately assess when they are empty without counting each dose. It illustrates the need for better devices to track doses remaining (an advantage of dry-powder inhalers).

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MEDICAL THERAPIES

DOUBLING THE DOSE OF INHALED CORTICOSTEROID TO PREVENT ASTHMA EXACERBATIONS: RANDOMISED CONTROLLED TRIAL


Purpose of the Study. The investigators proposed to determine if doubling the dose of inhaled corticosteroids (ICSs) to treat deteriorating asthma control reduced the need for starting oral corticosteroids.

Study Population. The study population included 390 nonsmoking individuals aged ≥16 years, with stable asthma requiring regular ICS use and a course of oral corticosteroids or doubled dose of ICS in the past 12 months.

Methods. Participants recorded their daily morning peak flow and daytime symptom score on a 4-point scale. After a 2- to 4-week run-in period, an independent pharmacist randomly allocated participants to receive active or placebo study inhalers, matched to their usual ICS, inhaler type, and dose. Patients were stratified into low-to-moderate–dose (equivalent of beclomethasone dipropionate, =1000 μg/day) and high-dose groups based on their dose of ICS at study entry. They continued their usual ICS and added the study inhaler for 14 days if their morning peak flow fell by 15% or their daytime symptom score increased by 1 point compared with the run-in period means. Participants took 10 days of oral prednisolone (30 mg/day) if their peak flow fell 40% from the mean run-in value or if their asthma control deteriorated to where they would usually start oral corticosteroids.

Results. Of the 192 participants in the active-inhaler group, 110 started their study inhaler (88 in the low-to-moderate–dose group), and of the 198 participants in the placebo-inhaler group, 97 started their study inhaler (74 in the low-to-moderate-dose group). Twenty-two participants (11%) in the active-inhaler group and 24 (12%) in the placebo group started prednisolone, for a risk ratio of 0.95 (95% confidence interval [CI]: 0.55, 1.64). Prednisolone was started because of a 40% peak-flow drop in 6 participants in the active group and 4 controls. In the low-to-moderate–dose group, 13 of 158 in the active group and 17 of 162 in the placebo group started prednisolone, for a risk ratio of 0.8 (95% CI: 0.4, 1.6). Doubling the dose of ICS led to a small reduction in the mean maximum fall of peak flow but did not change the time taken for peak flow or symptom scores to return to the baseline.

Conclusions. These findings do not support the effectiveness of doubling the dose of ICS to prevent the need for oral corticosteroids during asthma exacerbations.

Reviewers’ Comments. This randomized, control trial questions a recommendation that is part of many asthma-exacerbation-management plans. Although the results of at least 1 other study support these findings, a longer study following individuals beyond their first need for oral corticosteroids, involving larger increases as well as doubling of ICS doses, evaluating objective measures such as peak flow and symptom scores in all patients at the time of starting oral corticosteroids, and including younger patients and those with milder disease may reveal a benefit to increasing the ICS dose in some situations and subgroups of asthmatics. However, if this study’s findings can be consistently replicated in children, we may need to modify our recommendations for early management of asthma exacerbations.

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COST-EFFECTIVENESS ANALYSIS OF EARLY INTERVENTION WITH BUDESONIDE IN MILD PERSISTENT ASThma


Purpose of the Study. These investigators analyzed cost-effectiveness of a commonly prescribed inhaled corticosteroid from the perspectives of both direct and indirect costs.

Study Population. Patients aged 5 to 66 years from 32 countries were enrolled in the Inhaled Steroid as Regular Therapy in Early Asthma (START) study. Patients were eligible if they were diagnosed with asthma within 2 years of randomization and lacked significant comorbidity.

564 ASTHMA
How Do Patients Determine That Their Metered-Dose Inhaler Is Empty?
Mary Beth Bollinger

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