

Inhaled corticosteroids and allergy specialty care reduce emergency hospital use for asthma

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Background: The interrelationships between optimal inhaled corticosteroid (IC) therapy, allergy specialist care, and reduced emergency hospital care for asthma have not been well defined.

Objective: We sought to evaluate the independent effectiveness of various levels of IC dispensing and allergy specialist care in reducing subsequent emergency asthma hospital use.

Methods: Asthmatic patients (n = 9608) aged 3 to 64 years were identified from an electronic database of a large health maintenance organization. The outcome was any year 2000 asthma hospitalization or emergency department visit. The main predictors were at least one allergy department visit and the number of IC canisters dispensed in 1999. Analyses were adjusted for age, sex, insurance type, and asthma severity (1999 emergency asthma hospital use, β -agonist use, and oral corticosteroid use).

Results: Dispensing of 7 or more canisters of ICs (odds ratio [OR], 0.64; 95% CI, 0.43-0.94) and allergy care (OR, 0.73; 95% CI, 0.55-0.97) were associated with reduced subsequent emergency asthma hospital use. More patients with allergy specialist care than those without such care received 7 or more dispensations of ICs (24.7% vs 8.3%, $P < .001$). When 7 or more dispensations of ICs and allergy specialist care were simultaneously included in an adjusted model, both ICs (OR, 0.68; 95% CI, 0.46-1.00) and allergy care (OR, 0.77; 95% CI, 0.58-1.02) were independently associated with a lower risk of year 2000 emergency asthma hospital care, although significance was borderline.

Conclusion: Allergy care reduces emergency hospital use for asthma by increasing use of ICs but probably also has an independent effect. (J Allergy Clin Immunol 2003;111:503-8.)

Key words: Asthma, inhaled corticosteroids, allergist, hospitalization, specialist, emergency care

Randomized controlled clinical trials have shown that inhaled corticosteroids (ICs) reduce asthma symptoms and improve pulmonary function.^{1,2} However, few of these studies have the statistical power to evaluate an effect on less common but important outcomes, such as asthma hospitalizations or emergency department (ED)

Abbreviations used

ED: Emergency department

IC: Inhaled corticosteroid

visits. Therefore the data showing that ICs prevent emergency hospital use for asthma have generally been from nonrandomized studies.³

Several such studies have suggested that patients receiving ICs experienced fewer hospitalizations for asthma than patients not receiving such therapy,⁴⁻⁸ but other similar studies⁹⁻¹¹ did not confirm these results.

A major problem with evaluating asthma interventions in these nonrandomized studies is that the therapeutic choices have not been made randomly. Thus it is difficult to separate the effects of the intervention from the effects of disease severity and other factors related to that therapeutic choice.³ For example, a relationship between specialty care for asthma and the use of ICs has been suggested.¹²⁻¹⁸ The main purpose of this study was to explore the interrelationships between allergy specialty care, the dispensing of ICs, and the reduction of asthma emergency hospital use after adjusting for baseline demographic and asthma severity differences in an asthmatic population from a large group-model health maintenance organization.

METHODS

This study was approved by the Southern California Kaiser Permanente Institutional Review Board. Data for this study were derived from the Southern California Kaiser-Permanente Asthma Case Identification Database, which is based on linkage of computer data from a hospital discharge database; a diagnosis and procedures database; a membership database; and a prescription database. Patients are identified as having asthma if they meet one or more of the following criteria:

1. any discharge diagnosis (principal or other diagnosis) of asthma in the hospitalization database (ICD-9 code: 493.xx);
2. 2 or more asthma-related medication dispensations (excluding oral steroids) in a 1-year period in the prescription database, including β -agonists (excluding oral terbutaline), inhaled steroids, other inhaled anti-inflammatory drugs, and oral leukotriene modifiers; or
3. ED or regular clinic asthma-related visit appointment in the diagnosis and procedures database.

This algorithm is based on the evidence that identifying physician-diagnosed asthma is a valid way to identify asthmatic patients in epidemiologic studies.¹⁹ Physician-diagnosed asthma is captured explicitly by criteria 1 and 3 and implicitly by criterion 2.

Subjects in the present cohort were patients included in the Asthma Case Identification Database during 1999 and 2000 who were

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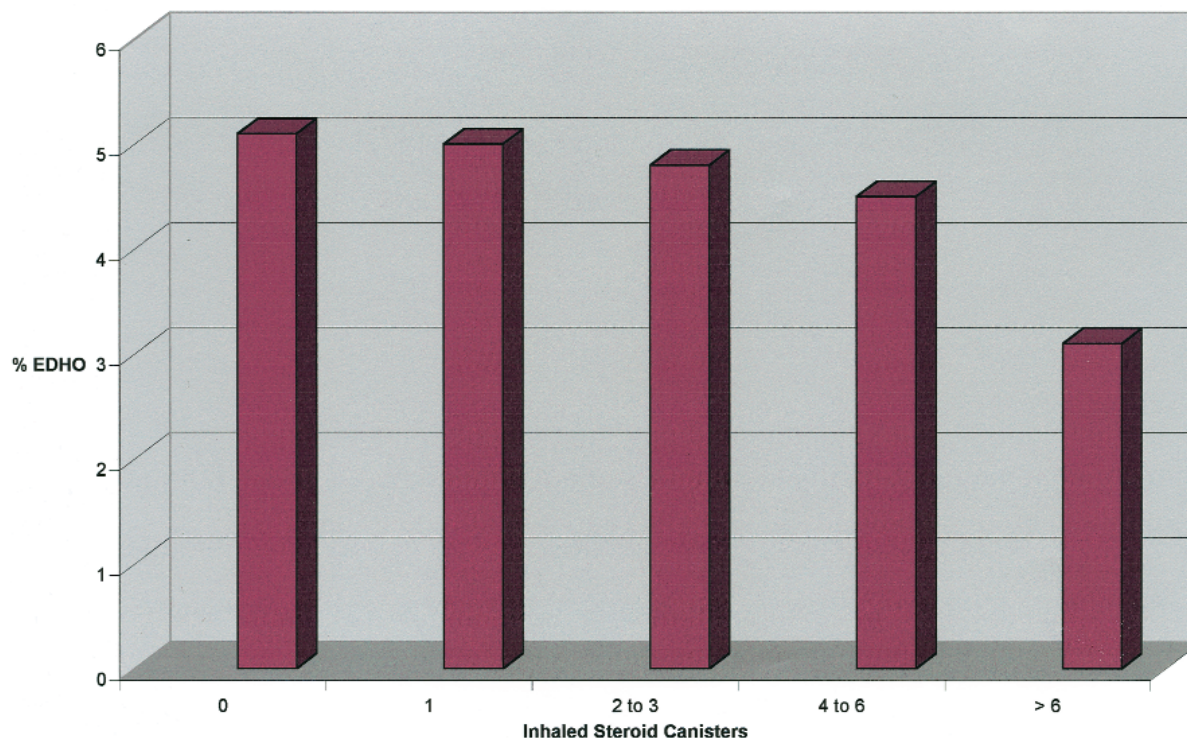


FIG 1. The relationship between the number of IC canisters used in 1999 and the likelihood of experiencing an asthma ED visit or hospitalization in the year 2000 (% EDHO).

aged 3 to 64 years, were assigned to the San Diego medical center, were continuously enrolled in 1999 and 2000, and had prescription drug coverage as a benefit. Potential subjects with a diagnosis of chronic obstructive pulmonary disease (ICD-9 codes 491.xx, 492.xx, or 496.xx) were excluded from the analysis to identify a purely asthmatic population. The outcome was emergency hospital use for asthma during the year 2000, which was defined as at least one hospitalization or ED visit for asthma (ICD-9 code 493.xx) expressed as a yes-or-no variable.

The predictors of interest were the number of canisters of an IC dispensed in 1999 and a visit to an allergy specialist in 1999. Potential demographic confounders included age, sex, and type of insurance (ie, commercial vs subsidized through Medicaid, Medicare, or other sources, a marker for lower socioeconomic status). The analyses were also adjusted for asthma severity on the basis of occurrence of at least one asthma ED visit or hospitalization in 1999, the number of short-acting β -agonist canisters dispensed in 1999, and the number of courses of oral corticosteroids dispensed in 1999.

All analyses were conducted with SAS version 8.2 for Windows software. Hypothesis testing for binary variables in unadjusted analyses was by means of the Fisher exact test for 2 predictors and by means of χ^2 analysis for more than 2 predictors. Hypothesis testing for differences in continuous variables between groups was by means of the Student *t* test. Multivariable analyses were conducted by using multiple logistic regression analyses. Hypothesis testing in logistic regression models was by means of Wald χ^2 testing. A 2-sided *P* value of less than .05 was considered statistically significant in univariate and multivariable analyses.

RESULTS

The final cohort included 9608 subjects, 0.7% of whom were hospitalized for asthma during 2000, 4.3% of

whom required an asthma ED visit during 2000, and 4.7% of whom required emergency hospital care in the form of at least one ED visit or hospitalization during 2000.

The occurrence of year 2000 emergency hospital care in relationship to baseline 1999 demographic, asthma severity, and treatment variables is shown in Table I. The likelihood of hospital care for asthma in the year 2000 decreased with age, increased in patients with subsidized insurance and 1999 emergency hospital care, and increased with more 1999 oral corticosteroid use. No significant relationships with sex or level of β -agonist use were demonstrated.

There appeared to be a trend toward decreased emergency hospital care with 1999 IC use of 4 or more canisters per year (Fig 1). Indeed, patients receiving 4 or more canisters per year of ICs were significantly less likely than patients receiving less than 4 canisters per year to experience subsequent emergency hospital care for asthma (odds ratio [OR], 0.76; 95% CI, 0.60-0.96), and patients receiving 7 or more canisters per year were even less likely than those receiving fewer canisters to require year 2000 emergency hospital care for asthma (OR, 0.61; 95% CI, 0.42-0.88). In a multivariable analysis (data not shown) forcing in baseline demographic and severity characteristics and offering levels of inhaled steroid canister use in 1999 of 1 or more through 8 or more canisters, dispensing of 7 or more canisters was the only IC variable that entered the model. Thus 7 or more canisters of ICs was chosen as the most effective level for use in subsequent analyses. Table I shows no significant rela-

tionship between allergist care and subsequent emergency hospital use for asthma in this unadjusted analysis (OR, 0.85; 95% CI, 0.64-1.11).

Differences between patients who received 7 or more canisters of ICs in 1999 and those receiving less than this amount are shown in Table II. Patients receiving 7 or more canisters were older and received more β -agonist canisters and oral steroid courses in 1999 than those using less than 6 canisters. No significant differences between groups were demonstrated for sex, type of insurance, or 1999 asthma ED visits or hospitalizations.

Differences between patients seeing an allergy specialist in 1999 and those not seeing an allergy specialist are also shown in Table II. Patients seeing an allergy specialist were more likely to have commercial (versus subsidized) insurance and had more severe asthma during 1999 reflected by more asthma ED visits or hospitalizations, β -agonist canisters, and oral steroid dispensations. A significant relationship is also demonstrated between dispensing of more than 7 canisters of ICs in 1999 and allergy specialty care in 1999 ($P < .001$).

The relationship between dispensing of 7 or more canisters of ICs in 1999 and emergency hospital asthma care in 2000 was evaluated in a forward stepwise logistic regression model that included baseline demographic and severity characteristics (Table III, model A). Dispensing of 7 or more canisters conferred significant protection (OR, 0.64), independent of the other predictors examined.

The relationship between allergy specialty care in 1999 and emergency hospital asthma care in 2000, after adjusting for baseline demographic and asthma severity characteristics, is shown in Table III, model B. In contrast to the crude analysis, this analysis shows that allergy care provided significant protection (OR, 0.73) against emergency hospital care the following year after adjusting for other baseline risk factors.

The relationship between use of 7 or more canisters of ICs and allergy specialty care in 1999 in protecting against emergency hospital use for asthma in the year 2000 was investigated in a model that also included the baseline demographic and asthma severity predictors (Table III, model C). The ORs for both interventions were higher (less effect) than when only one intervention was included in the model (Table III, models A and B), which would be expected given the collinearity of these 2 variables. However, the independent contribution of ICs (OR, 0.68) was barely significant, and the independent contribution of allergy specialty care (OR, 0.77) was nearly significant in this model (Table III, model C). There was no statistical evidence of an interaction between IC use and allergy care in these models (data not shown). Consistent with independent and additive effects of optimal IC therapy and allergy care, patients with both interventions ($n = 380$) had a lower rate of year 2000 emergency hospital use (2.9%) compared with rates of patients ($n = 666$) with only inhaled steroids (3.2%), patients ($n = 1156$) with only allergy care (4.5%), and patients ($n = 7406$) with neither intervention (5.0%). However, the statistical significance of these differences was only borderline ($\chi^2 = 7.62$, $P = .055$).

TABLE I. Relationship of baseline 1999 demographic, severity, and treatment characteristics to year 2000 emergency hospital care for asthma

Characteristic	No. (%)	EDHO (%)	P value (χ^2)
Age			<.0001
3-5	665 (6.9)	8.0	
6-10	1203 (12.5)	6.7	
11-17	1430 (14.9)	5.5	
18-35	1823 (19.0)	4.7	
36-50	2467 (25.7)	4.1	
51-64	2020 (21.0)	2.6	
Sex			.592
Male	4305 (44.8)	4.6	
Female	5303 (55.2)	4.8	
Commercially insured			<.0001
Yes	9046 (94.2)	4.5	
No	562 (5.9)	8.2	
1999 EDHO			<.0001
Yes	650 (6.8)	14.0	
No	8958 (93.2)	4.0	
β -agonist*			.254
0	1514 (15.8)	5.7	
1-2	2618 (27.3)	4.5	
3-5	1840 (19.2)	4.5	
6-11	1901 (19.8)	4.2	
>11	1735 (18.1)	5.0	
Oral steroids†			<.0001
0	6560 (68.3)	3.6	
1-2	2609 (27.2)	6.0	
>2	439 (4.6)	10.7	
Inhaled steroids*			.087
0	4283 (44.6)	5.1	
1	1061 (11.0)	5.0	
2-3	1849 (19.2)	4.8	
4-6	1369 (14.3)	4.5	
>6	1046 (10.9)	3.1	
Allergist care			.223
Yes	1536 (16.0)	4.1	
No	8072 (84.0)	4.8	
Total	9608 (100)	4.7	

EDHO, Year 2000 emergency hospital care for asthma.

*Short-acting β -agonists, canisters per year.

†Dispensations per year.

DISCUSSION

Asthma hospitalizations and ED visits not only represent undesirable patient outcomes, but they also account for \$2.6 billion per year of direct medical costs.²⁰ Interventions shown to be effective in preventing such events are thus very important. Randomized controlled trials of asthma interventions do not usually have sufficient power to evaluate emergency hospital care as an outcome. Thus data showing that asthma interventions reduce emergency hospital care most often come from nonrandomized observational studies.

One approach has been to use a pre-post cohort design. For example, ICs reduced the hospitalization rate by 50% in 36 subjects with severe steroid-dependent asthma in the 2 years after treatment compared with in the 2 years before treatment.²¹ Similarly, Westley and Spiecher²² reported that allergist care reduced asthma

Asthma, rhinitis,
other respiratory
diseases

TABLE II. Relationship of dispensing of 7 or more canisters of inhaled steroid or allergy care during 1999 to other 1999 baseline characteristics

Parameter	ISC7			Allergy care		
	Yes	No	P value	Yes	No	P value
No.	1046	8562	—	1536	8072	—
Age*	42.5 (0.5)	30.1 (0.2)	<.001	31.0 (0.5)	31.5 (0.2)	.35
Female sex	56.5%	55.0%	.37	53.7%	55.5%	.21
Commercial†	94.2%	94.2%	1.00	95.8%	93.8%	.003
ED/hospital‡	6.7%	6.8%	1.00	8.9%	6.4%	<.001
β-agonists§	11.1 (0.3)	5.7 (0.1)	<.001	7.5 (0.2)	6.0 (0.1)	<.001
Oral steroid	0.82 (0.05)	0.50 (0.01)	<.001	0.92 (0.03)	0.46 (0.01)	<.001
Allergy care	36.3%	13.5%	<.001	—	—	—
ISC7	—	—	—	24.7%	8.3%	<.001

ISC7, Dispensing of 7 or more canisters of IC.

*Mean years (SEM).

†Commercial versus subsidized insurance.

‡Asthma ED visit or hospitalization.

§Short-acting β-agonists, mean canisters per year (SEM).

||Mean courses per year (SEM).

TABLE III. Multivariable models for asthma ED visits or hospitalizations in the year 2000 with more than 7 canisters of ICs during 1999, allergy care during 1999, or both as predictors

Predictor	OR (95% CI)		
	Model A	Model B	Model C
Age	0.99 (0.98-0.99)	0.98 (0.98-0.99)	0.98 (0.98-0.99)
Female sex	1.24 (1.02-1.52)	1.25 (1.02-1.52)	1.24 (1.02-1.52)
1999 asthma ED visit/hospitalization	3.10 (2.40-4.02)	3.13 (2.42-4.06)	3.11 (2.40-4.04)
1999 β-agonist canisters	1.01 (1.00-1.02)	1.01 (1.00-1.02)	1.01 (1.00-1.02)
1999 oral steroid courses	1.14 (1.06-1.23)	1.14 (1.06-1.23)	1.15 (1.07-1.24)
Commercial insurance	0.55 (0.40-0.76)	0.56 (0.40-0.77)	0.56 (0.40-0.77)
ISC7	0.64 (0.43-0.94)	—	0.68 (0.46-1.00)
Allergy care	—	0.73 (0.55-0.97)	0.77 (0.58-1.02)

ISC7, Dispensing of more than 7 canisters of ICs during 1999.

hospitalizations by 67% in 70 patients compared with numbers in the year before they received allergist care. However, because of the absence of a concurrent reference group, it is impossible to know whether asthma severity might have decreased over time, even without the benefit of the intervention examined.³

Another approach is comparing asthma hospitalizations in treated versus nontreated individuals in cohort studies.⁴⁻¹¹ As noted previously, cohort studies regarding the effect of inhaled steroids on asthma hospitalizations have been conflicting. A number of cohort studies have suggested that allergy specialist care reduces asthma ED visits, hospitalizations, or both.^{12,13,15,17,18,23} Although therapeutic interventions were not randomized in these studies, most of them did attempt to account statistically for baseline differences between groups. A major advantage of these types of cohort studies is that they usually reflect outcomes in real-world settings better than randomized controlled trials.

The current cohort study suggests that patients who received 4 or more canisters of ICs per year required significantly less emergency hospital care for asthma the next year than those who received less than 4 canisters per year. The data also suggest that use of 7 or more canisters per year had the strongest independent effect after

adjusting for potential confounders (OR, 0.64). Similarly, in a large cohort of patients (n = 30,569), Suissa et al²⁴ have recently reported that use of 6 or more canisters of ICs per year reduced deaths caused by asthma compared with use of less than 4 canisters per year. One potential application of this information is in determining the adequacy of IC therapy in database asthma surveillance. Our data and those of Suissa et al²⁴ suggest that 4 or more canisters per year would be the minimally adequate amount and that 6 to 7 or more canisters might be a more consistently effective threshold. It should be noted that during the years of this study, most subjects in this population used inhaled chlorofluorocarbon-beclomethasone (42 μg per puff) or chlorofluorocarbon-triamcinolone. It is possible that use of higher-potency steroids would decrease the effective canister level threshold.

Allergy specialty care in this study did not demonstrate protection against subsequent emergency hospital asthma care in unadjusted analyses. This was probably because of baseline demographic differences and increased asthma severity in patients seen by allergists (Table II). After adjusting for these factors, allergy care for asthma provided a significant protection (OR, 0.73) against emergency care the following year.

Although prior studies and the current study have shown that both ICs and allergy care reduce emergency hospital use, no prior study has evaluated the relationship between these 2 interventions in reducing adverse asthma outcomes. A relationship between these 2 interventions has been reported in prior studies¹²⁻¹⁷ and confirmed in this study. Patients receiving allergy care in the current study were 3 times more likely to use 7 or more canisters of ICs than patients not seen in the allergy department (Table II). However, the current study extends prior observations by showing that ICs and allergy specialty care have independent and additive effects in reducing emergency hospital use for asthma. When both allergy care and ICs were concurrently evaluated in this study, adjusting for possible confounders (Table III, model C), each demonstrated less effect than when evaluated alone (Table III, models A and B), but the independent effect of ICs was significant, and that of allergy specialty care was nearly so. Moreover, patients with both interventions experienced the lowest incidence of subsequent emergency hospital use compared with patients with either or neither intervention. These findings suggest that an important component of the effect of allergist care on reducing emergency hospital use for asthma is due to increased prescribing of and adherence to ICs. However, these data also suggest that other aspects of allergy care, such as patient education, environmental control, use of other medications, and immunotherapy, might contribute to this effect as well.²⁵

We have previously reported the results of a clinical trial in 309 patients presenting to our ED with acute asthma in which patients were alternatively assigned to facilitated allergist referral or usual care.¹² In that study allergist referral led to reduced nocturnal symptoms, reduced ED relapses, and greater use of ICs compared with usual care. The current study extends those observations in 3 ways. First, it confirms reduced emergency hospital use associated with allergist care in a larger number of unselected patients. Second, it shows that in the nonclinical trial setting allergists see patients with more severe disease. Finally, and most importantly, it shows that, even after adjusting for baseline severity and IC use, allergist care still reduces emergency hospital use for asthma.

As noted above, not all prior cohort studies have been able to show that IC use reduces emergency hospital care for asthma. Part of the explanation for this variability might be that IC use is not only an effective intervention but also a marker of severity in population studies. As a marker of severity, it would have a positive, rather than an inverse, relationship with emergency hospital care for asthma. Differences in asthma severity and other clinical factors between study populations might determine whether IC use functions more as an effective intervention or as a marker of severity in a given study and thus whether IC use can be shown to reduce emergency hospital use for asthma.

The internal validity of this study was strengthened by a number of factors. It was population based and included a relatively large number of asthmatic patients. It used

an objective measure of determining the number of IC canisters dispensed rather than relying only on patient reporting, which is frequently inaccurate.²⁶ It evaluated a dose-response relationship between the use of ICs and emergency hospital care rather than using only 2 or 3 dose categories, as used in many prior studies.^{5-9,27} The study design ensured that the intervention occurred before the outcome. Finally, this study adjusted for a number of important demographic and severity confounders previously shown to be related to emergency hospital use for asthma in this type of population.^{9,27}

This study does have several limitations. Dispensing of medication does not automatically equate to use of medication, although pharmacy records are being recommended as a method of assessing patient adherence.^{28,29} One cannot directly extrapolate canisters per year of ICs from this study to an adequate daily dose because patients might have started therapy at different times during 1999 and because of differences between puffs per canisters and potencies of the different ICs used. The inability to determine when in 1999 patients used their ICs or had their allergy care also makes it impossible to determine a relationship in this study between timing of these interventions (eg, earlier in the year vs later) and subsequent year 2000 emergency hospital use. This study also did not capture unscheduled outpatient visits other than ED visits, although ED visits would be the most expensive type of outpatient unscheduled asthma visits.

A final issue is the external validity of this study. Patients receiving care from San Diego Kaiser Permanente are demographically similar to the Southern California working family population (unpublished data). However, the asthma hospitalization and ED rate was quite low compared with levels reported in other populations.^{18,30} This might be related to the access of this population to routine care, telephone interactions, urgent appointment clinics, and specialty care. The results of this study should be generalizable to populations with similar health care access but might not be generalizable to other populations.

In summary, this study demonstrates that both adequate IC therapy and allergy specialty care are effective interventions in the prevention of emergency hospital care for asthma. Although the current data confirm that there is a definite relationship between these 2 interventions in asthmatic populations with access to allergy care, the data also suggest that these interventions are probably independently effective as well. Finally, this study provides guidance regarding the determination of adequate IC therapy for use in asthma population management.

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