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ORIGINAL RESEARCH

Inhaler device, administration technique, and adherence to inhaled corticosteroids in patients with asthma

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Abstract

Aim: To compare inhaled corticosteroid (ICS) inhaler type with user technique and ICS medication adherence among adults with asthma.

Methods: We classified 270 adults into two groups by ICS device type: metered-dose inhaler (MDI) or dry powder inhaler (DPI). Inhaler technique was assessed using standardised checklists. Medication adherence was evaluated using the Medication Adherence Report Scale (MARS). Differences in inhaler technique and MARS score among patients using MDIs versus DPIs were evaluated.

Results: Univariate analysis showed no difference in technique scores between the groups (p=0.46), but better ICS adherence among DPI users (p=0.001). In multivariable analysis, DPI use remained significantly associated with higher rates of adherence (OR 2.2; 95% CI 1.2 to 3.8) but not with inhaler technique (–0.2; 95% CI –0.5 to 0.1) after adjusting for potential confounders.

Conclusions: Type of inhaler device appears to be associated with adherence to asthma controller medications. Prospective studies are needed to elucidate further the potential effect of the type of ICS delivery device on asthma self-management.

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See linked editorial by Horne on pg 118

Introduction

Asthma is a significant public health problem, particularly among inner city populations.[1-5] It is a leading cause of preventable emergency room visits and hospitalisations.[6] Considerable efforts have been directed at promoting appropriate self-management behaviours in order to improve asthma outcomes.[7] Inhaled corticosteroids (ICS) are a particularly critical component of these efforts. It has been estimated that regular use of ICS could reduce asthma hospitalisations by as much as 80%,[8] and that the risk of death from asthma decreases by 21% for each additional ICS canister used in the previous year.[9] Despite such potential, patients with asthma appear to adhere poorly to prescribed ICS medications.[10,11]

There have been many delivery systems developed for ICS, each with advantages and disadvantages.[12] Among these, the two most frequently used devices are the pressurised metered-dose inhaler (MDI) and the dry powder inhaler (DPI). For ICS to be effective, good inhaler technique and adequate adherence are important. With regard to technique, specific steps and good coordination are necessary for the proper use of these devices. A less than optimal technique can result in decreased drug delivery and potentially reduced efficacy.[11,13,14] Large systematic reviews of bioequivalence have found that, when properly used, MDI and DPI devices are no different in delivering inhaled medications.[11,12,15] However, most of these studies compared inhaler devices in controlled environments where patients

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received structured education on proper inhalation technique and were monitored to ensure proper use. The importance of the type of device in inhaler technique and drug delivery in routine care is unclear.[14,16-19]

Effective use of ICS also requires good medication adherence, a critical component of self-management. Suboptimal adherence to ICS is a major contributor to poor asthma outcomes.[9,20] Some factors influencing adherence include disease and medication beliefs, access to medical care, and relationship with health care provider.[21-26] Studies examining the association between ICS device type and medication adherence are limited, especially among inner city minority populations.[27-29] Thus, additional data are necessary to assist physicians in evaluating the potential impact of the type of device prescribed on the self-management behaviour of patients.

The objective of our study was to examine the association between ICS device, ICS administration technique, and medication adherence among inner city asthmatic patients treated in the community. Our primary research question was whether patients using a Diskus delivery device were more adherent to their ICS than patients using an MDI delivery device, and our secondary question was whether patients using a Diskus delivery device had better technique than patients using an MDI device.

Methods

Patient population

We analysed data collected as part of a cohort study of adults with persistent asthma followed at hospital-based clinics in two inner city locations: East Harlem, New York City and New Brunswick, New Jersey.[30] Study participants were enrolled over a 33-month period from July 2004 to March 2007. The clinic's computerised registration system of both medical centres was scanned daily to identify adult patients with a physician diagnosis of asthma. Patients were eligible if they were ≥18 years old; spoke English or Spanish; and had persistent, moderate, or severe asthma as defined by the National Heart, Lung, and Blood Institute guidelines. Individuals with a smoking history of ≥10 pack-years or other chronic respiratory illness were excluded. For purposes of this study, only patients on an ICS for asthma treatment were included in the analyses. The Institutional Review Boards of Mount Sinai School of Medicine and Robert Wood Johnson School of Medicine approved the study. Written informed consent was obtained from all participants.

Data collection and measurements

Trained research staff conducted interviewer-administered surveys in English or Spanish. The Spanish translation of the survey instrument was back-translated into English, and the original and back-translated versions were compared to confirm their equivalence across languages.

The primary predictor of interest was the type of ICS delivery device used (DPIs vs. MDIs). DPIs are 'breath-actuated' devices providing drug only when demanded by patient inhalation. They are flow-dependent and necessitate moderate to high inspiratory flow in order to deliver medication adequately but require minimal patient/device coordination.[14] Conversely, MDIs are not flow-dependent and require coordination of actuation at the time of inspiratory flow for adequate deposition of medication in the lung. Patients were classified as using DPI versus MDI inhaler devices based on self-reported data and by reviewing all asthma medications during the in-person interview.

The first outcome of interest was technique of ICS administration. Inhalation technique was assessed by asking participants to demonstrate how they use their asthma inhalers with a placebo device. All study patients used an MDI for their short-acting β-agonist medications and many also used an MDI for ICS. Thus, all participants were asked to demonstrate use of an MDI device. In addition, patients using a DPI were asked to demonstrate how they used this device. Inhalation technique scores were assessed using instruments adapted from validated standardised checklists specific to each device (Table 1).[31-33] The technique was scored on an 8-point and 7-point scale for the MDI and DPI devices, respectively, with higher scores indicating better technique.

The second outcome of interest was medication adherence. The Medication Adherence Report Scale for Asthma (MARS), a 10-item instrument previously validated against objective measures of adherence (electronic monitoring), was used to assess adherence among study participants.[34] The MARS measures intentional as well as non-intentional non-adherence and is available in both English and Spanish. Medication use is rated on a 5-point Likert scale, with higher scores indicating better adherence. Consistent with previous studies, patients were considered 'adherent' if their MARS score was >4.5.[22,31,34]

Table 1. Checklists used to assess inhaler technique.

Metered dose inhaler	Dry powder inhaler
1. Shake the inhaler and remove protective cap	1. Prepare the inhaler before usage
2. Hold inhaler upright	2. Keep inhaler horizontal
3. Exhale to residual volume	3. Exhale to residual volume
4. Place mouthpiece between lips and teeth	4. Place mouthpiece between lips and teeth
5. Inhale slowly and simultaneously active the canister	5. Inhale forcefully and deeply
6. Continue slow and deep inhalation	6. Take the inhaler out of the mouth
7. Hold breath for 5–10 s	7. Hold breath for 5 s
8. Take inhaler out of mouth and hold breath for 5–10 s	

Statistical analysis

In order to compare MDI and DPI scores we first calculated the percentage of steps that patients performed correctly for each device. We then converted these percentages into a standard normal variable so that differences in scores were equivalent among scales. The final ICS technique score was defined as the standardised DPI score for DPI users and the standardised MDI score for MDI users.

The characteristics of DPI and MDI users were compared using the χ^2 test, the Wilcoxon rank sum test, or a t-test as appropriate. Descriptive analyses assessing proper device technique were performed, examining the percentage of patients completing each step for both devices. The univariate association between device type and the two outcomes – ICS technique score and medication adherence – were assessed using a t-test and χ^2 test, respectively. Primary analyses compared ICS technique scores among MDI and DPI users. In secondary analyses the MDI scores were compared between the two groups. Additionally, in an analysis limited to DPI users, each patient's DPI and MDI scores were compared using a paired t-test. The secondary analyses were performed to assess whether potential differences in technique were device-specific or due to differences in the characteristics of the patients prescribed these devices.

We conducted multivariable analyses to examine if device type was associated with inhaler technique and/or medication adherence using linear regression and logistic regression, respectively. The models were adjusted for age, gender, race/ethnicity, native language (English or Spanish), education, income, insurance status, emergency department visits and

Table 2. Characteristics of asthma patients according to type of device used for inhaled corticosteroid delivery.

Characteristic	Total (n=270)	MDI users (n=107)	DPI users (n=163)	p value*
Mean±SD age, years	48.2±13	49.1±13	47.6±14	0.34
Female, n (%)	220 (82)	85 (79)	135 (83)	0.42
Ethnicity, n (%)				
White	27 (11)	11 (11)	16 (11)	0.69
Black	77 (30)	30 (29)	47 (31)	
Hispanic	150 (59)	62 (60)	88 (58)	
Other	2 (1)	0 (0)	2 (1)	
Native language English, n (%)	164 (61)	65 (61)	99 (61)	0.97
High school graduate, n (%)	96 (36)	39 (36)	57 (35)	0.83
Income, n (%)				
<$5,000	59 (22)	25 (24)	34 (21)	0.06
$5,000–14,999	109 (41)	48 (45)	61 (38)	
$15,000–29,999	33 (12)	13 (12)	20 (12)	
$30,000–50,000	27 (10)	3 (3)	24 (15)	
>$50,000	22 (8)	10 (9)	12 (7)	
Don't know or refused	18 (7)	7 (7)	11 (7)	
Insurance status, n (%)				
Medicaid only	169 (63)	62 (58)	107 (66)	0.26
Medicare only/Medicaid and Medicare	55 (20)	27 (25)	28 (17)	
Other	45 (17)	18 (17)	27 (17)	
Asthma history				
Mean±SD age of onset, years	22.2±18	22.8±18	21.5±18	0.44
Mean±SD emergency department visits†	2.0±3	1.4±2	2.7±4	0.04
Mean±SD hospital admissions†	1.1±3	0.6±1	1.5±3	0.09
Mean±SD outpatient visits†	1.8±3	1.4±2	2.2±3	0.12
Oral steroids, n (%)†	204 (76)	70 (66)	134 (82)	0.002
Ever intubated, n (%)	30 (11)	11 (11)	19 (12)	0.75
Co-morbid conditions, n (%)				
Seasonal/nasal allergies	174 (65)	71 (66)	103 (64)	0.64
Gastro-oesophageal reflux disease	103 (38)	40 (37)	63 (39)	0.80
Diabetes	67 (25)	27 (25)	40 (25)	0.92
Hypertension	131 (49)	53 (50)	78 (48)	0.82
Depression	126 (47)	56 (52)	70 (43)	0.14

DPI=dry powder inhaler; MDI=metered-dose inhaler.

*Characteristics of DPI and MDI users were compared using the χ^2 test, Wilcoxon rank sum test, or t-test as appropriate

† During the previous year.

hospital admissions during the prior year, and oral steroid use. Beta coefficients and odds ratios are presented with 95% confidence intervals (CIs). All analyses used two-tailed significance levels of $p<0.05$ and were conducted with SPSS statistical software (SPSS Inc, Chicago, IL, USA).

Results

Between June 2004 and March 2007, 1,435 patients with ICD-9 codes for asthma were identified. Of these patients, 1,054 were excluded due to history of smoking for ≥10 pack-years (n=180, 17%), mild intermittent asthma severity (n=232, 22%), no history of asthma (n=316, 30%), cognitive impairment (n=2, 4%), other chronic lung diseases (n=179, 17%), and other reasons (n=105, 10%). Of the remaining 381 eligible patients, 55 (14.4%) did not participate in the study, leaving a cohort of 326 patients. Of the 326 enrolled in the study, 56 (17%) did not report being on an ICS, leaving a study cohort of 270 patients. Of these 270 participants, 163 (60%) used a DPI for ICS delivery and 107 (40%) used an MDI.

The mean±SD age of the participants was 48.2±13.3 years. Consistent with other inner city studies of asthma, most patients were female (82%) and belonged to minority ethnic groups (59% Hispanic and 30% Black). As shown in Table 2, sociodemographic characteristics were similar among the DPI and MDI groups ($p>0.05$ for all comparisons). Participants using DPI had more emergency department visits ($p=0.04$) and were more likely to require oral steroids ($p=0.002$) in the previous year. There were no differences in age of asthma onset, history of intubation, number of asthma outpatient visits in past year, or number of hospital admissions in past year ($p>0.05$ for all comparisons). Type of inhalation device was not associated with any of the co-morbid conditions assessed in the survey ($p>0.10$ for all comparisons).

Certain steps in proper device technique were commonly omitted (see Figures 1 and 2). Among MDI users, the steps least often completed were exhalation to residual volume prior to putting the inhaler in the mouth (50%) and holding the breath for 5–10 s after removal of the inhaler (47%). Among DPI users, the steps least often completed were exhalation to residual volume prior to putting the inhaler in the mouth (32%) and holding the breath for 5 s after removal of the inhaler (47%). The results of univariate analyses showed that the standardised ICS technique score was similar among MDI and DPI users (0.08 vs. –0.01, $p=0.46$; Table 3). In addition, when the analyses were limited to the MDI scores for all patients, the two groups also had similar scores (0.09 vs. 0.02, $p=0.58$). Analyses limited to DPI users showed no significant difference in standardised MDI and DPI scores when compared within each patient (mean difference 0.03, 95% CI –0.14 to 0.21, $p=0.69$). However, participants using DPI were more likely than MDI users to be adherent to their ICS (61% vs. 39%, $p=0.001$).

Figure 1. Percentage of patients correctly performing each step for metered dose inhaler use.

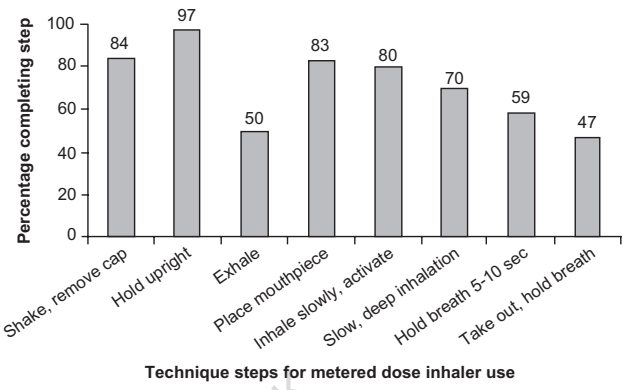
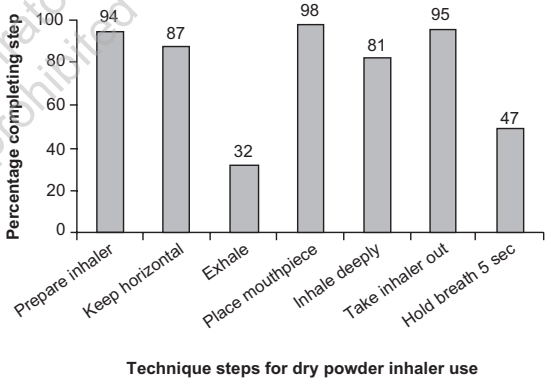


Figure 2. Percentage of patients correctly performing each step for dry powder inhaler use.



Multivariable analysis showed no significant association between device type and standardised ICS technique score (–0.2; 95% CI –0.5 to 0.1; Table 4), while DPI use remained significantly associated with higher rates of adherence (OR 2.2; 95% CI 1.2 to 3.8) after controlling for age, gender, race/ethnicity, native language, education, income, insurance status, emergency department visits during the previous year, hospital admissions during the previous year, and oral steroid use during the previous year.

Discussion

Asthma is a common chronic illness that is associated with significant morbidity among inner city patient populations. ICS remain the most important treatment for patients with persistent asthma.[7] However, inappropriate inhaler technique and poor adherence are frequent barriers to adequate control for these patients. In this study we examined the association

Table 3. Results of univariate analyses comparing inhaler technique and adherence scores according to device used for inhaled corticosteroid delivery.

Outcome	MDI users	DPI users	p value
Mean±SD standardised ICS technique score*	0.08±1.0	?0.01±1.0	0.46
Mean±SD standardised MDI score†	0.09±1.0	0.02±1.0	0.58
Adherent to ICS (%)‡	39.3	60.9	0.001

DPI=dry powder inhaler; MDI=metered-dose inhaler.

* Standardised inhaler technique scores were compared between MDI and DPI groups using a t-test. Standardised scores were calculated by subtracting the mean and thus are centred around 0.

† MDI scores were obtained for all participants irrespective of device used and the difference between the groups was compared using a t-test.

‡ Adherence was defined as a Medication Adherence Response Score >4.5 and the difference between the groups was compared using the χ^2 test.

Table 4. Results of multivariable analyses examining the association between inhaled corticosteroid device, inhaler technique, and medication adherence.

Variable	Inhaler technique	*Medication adherence†
	β coefficient (95% CI)	Odds ratio (95% CI)
Inhaled corticosteroid device		
Metered-dose inhaler	Reference	Reference
Dry powder inhaler	–0.2 (–0.5 to 0.1)	2.2 (1.2 to 3.8)
Age	–0.0 (–0.0 to 0.0)	1.0 (0.9 to 1.0)
Female	–0.2 (–0.7 to 0.3)	0.8 (0.4 to 1.8)
Race/ethnicity		
White	Reference	Reference
Black	–0.2 (–0.7 to 0.3)	0.7 (0.2 to 2.5)
Hispanic	–0.1 (–0.5 to 0.4)	0.5 (0.2 to 1.5)
Native language English	0.0 (–0.4 to 0.4)	0.7 (0.3 to 1.4)
High school graduate	0.2 (–0.1 to 0.5)	1.8 (1.0 to 3.3)
Income		
<$5,000	Reference	Reference
$5,000–14,999	–0.0 (–0.4 to 0.3)	1.3 (0.6 to 2.7)
$15,000–29,999	–0.1 (–0.6 to 0.4)	1.2 (0.5 to 3.2)
$30,000–50,000	0.2 (–0.3 to 0.8)	2.6 (0.7 to 9.2)
>$50,000	–0.2 (–0.9 to 0.6)	4.9 (1.0 to 23.2)
Insurance		
Medicaid Only	Reference	Reference
Medicare only/Medicaid and Medicare	?0.0 (–1.5 to 1.5)	1.2 (0.1 to 13.8)
Other	0.2 (–0.3 to 0.6)	0.5 (0.2 to 1.6)
Emergency department visits in previous year	–0.0 (–0.1 to 0.0)	1.1 (0.9 to 1.2)
Hospital admissions in previous year	0.2 (–0.1 to 0.5)	1.2 (0.6 to 2.2)
Oral steroid use in previous year	0.0 (–0.3 to 0.4)	0.8 (0.4 to 1.7)

*Linear regression analysis. †Logistic regression analysis.

between type of ICS device used, medication administration technique, as well as medication adherence among patients with asthma in ethnic minority groups. We found that certain steps in proper device technique are often omitted. Our results also showed that the type of device was not associated with inhaler technique scores, but there were higher rates of adherence among patients using a DPI. Further studies are necessary to establish prospectively the relationship between type of inhaler and ICS adherence.

Inhaler devices can affect appropriate use of ICS via two mechanisms – technique and adherence. First, proper technique is necessary in order to achieve adequate delivery of ICS to the lungs. Previous studies examining type of device and inhaler technique in real-life settings have had mixed results.[14,16-19] Consistent with our results, some previous studies have shown no difference in technique between various device types.[18,19] However, some studies showed that MDI users had worse techniques than users of other delivery devices.[14,16,17] None of the previous studies have focused on a population of primarily inner city patients belonging to minority ethnic groups who are at higher risk of poor asthma outcomes. Moreover, we were able to show no difference in MDI and DPI scores using patients as their own controls.

The second mechanism by which the type of device can affect efficacy of ICS is its potential influence on adherence. There are several device-related factors that may influence patient preference and adherence including ease of use, presence of a counter to track residual doses, and portability.[27,28] Another factor that may influence adherence is differences in the type of medication contained in the inhaler device. Most DPIs (at the time of this study) contained a combination of ICS plus a long-acting β-agonist (LABA); conversely, MDIs contained ICS alone. The bronchodilatory effect of LABAs may have influenced perceived effectiveness and consequently adherence. There are limited data in the literature about inhalation device type and patient adherence. Our results are consistent with those of Sheth *et al*. who compared adherence among DPI and MDI users using diary cards.[27] In this study of 154 patients with asthma, adherence was significantly higher with DPI than with MDI (91% vs. 79%; p=0.013). Conversely, Chapman *et al*. examined adherence in 37 adults with symptomatic but reversible obstructive airways disease through use of diary cards and found slightly lower adherence with DPI than with MDI (87% vs. 95%).[28] In comparing compliance among users of the Autohaler (similar to DPI) and MDI, Van Schayck *et al*. found no difference between the two (p=0.317).[29] The body of literature

examining adherence and device type is limited and contradictory; further studies are needed to establish the association. Our study extends these results by examining these associations in a larger cohort of inner city asthmatic patients.

These results have important implications for physicians managing patients with asthma. ICS adherence is one of the most important self-management behaviours for patients with asthma. Thus, maximising adherence as well as other self-management behaviours should be a priority for asthma providers. Many factors should be considered when prescribing an ICS, such as the patient's ability to use the device correctly, patient preferences, and availability of the desired drug in a particular inhaler device. It is important to partner with asthma patients to identify the medication that will meet their individual needs and thereby potentially improve adherence. Thus, if validated in prospective studies, these results suggest that physicians should consider type of delivery device as one of the potential factors that may determine adherence when prescribing ICS.

This study has strengths and limitations worth noting. The study focused on inner city patients with asthma, a group of patients at higher risk of poor outcomes. However, the study sample was enrolled from two hospital-based outpatient clinics and therefore the findings may not be representative of other centres or patients without regular access to care. Although we excluded patients with intermittent asthma, persistent asthmatics are the most important group to target with regard to improving ICS adherence since those with intermittent asthma are generally not on controller medications such as ICS. Use of an MDI compared with a DPI in the study population was determined by patients and providers. Importantly, most patients on a DPI in the study were on the combination of an ICS and a LABA; it is therefore likely that DPI users had more severe disease, a factor that may influence adherence. Although we adjusted for sociodemographic factors and several measures of severity on the multivariable analyses, we cannot exclude the possibility that potential differences in the baseline characteristics of these patients may explain the association between type of device and medication adherence. Additionally, the observed association may be related to differences in the medication included in these inhalers and not device-specific.

In summary, we found that, although DPIs were not associated with better inhaler technique, adherence to ICS was higher among patients treated with DPIs. Future studies should evaluate prospectively whether this association can translate into improved self-management among patients with persistent asthma.

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Conflicts of interest

Dr Juan Wisnivesky has received a research grant from GlaxoSmithKline and is a member of the research advisory board of EHE International. The other authors have no conflicts of interest to disclose.

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