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Assessment of Handling of Inhaler Devices in Real Life: An Observational Study in 3811 Patients in Primary Care

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ABSTRACT

The correct use of inhalation devices is an inclusion criterion for all studies comparing inhaled treatments. In real life, however, patients may make many errors with their usual inhalation device, which may negate the benefits observed in clinical trials. Our study was undertaken to compare inhalation device handling in real life. A total of 3811 patients treated for at least 1 month with an inhalation device (Aerolizer®, Autohaler®, Diskus®, pressurized metered dose inhaler (pMDI), or Turbuhaler®) were included in this observational study performed in primary care in France between February 1st and July 14th, 2002. General practitioners had to assess patient handling of their usual inhaler device with the help of a checklist established for each inhaler model, from the package leaflet. Seventy-six percent of patients made at least one error with pMDI compared to 49–55% with breath-actuated inhalers. Errors compromising treatment efficacy were made by 11–12% of patients treated with Aerolizer®, Autohaler,® or Diskus® compared to 28% and 32% of patients treated with pMDI and Turbuhaler®, respectively. Overestimation of good inhalation by general practitioners was maximal for Turbuhaler® (24%), and lowest for Autohaler® and pMDI (6%). Ninety percent of general practitioners felt that participation in the study would improve error detection. These results suggest that there are differences in the handling of inhaler devices in real life in primary care that are not taken into account in controlled studies. There is a need for continued education of prescribers and users in the proper use of these devices to improve treatment efficacy.

Key words: asthma, COPD, device, inhaler, misuse, primary care

INTRODUCTION

THE INHALED ROUTE OF ADMINISTRATION is widely accepted as being the best way of delivering drugs for the treatment of asthma or chronic obstructive pulmonary disease (COPD). It allows drugs to reach high bronchial concentrations and minimizes systemic bioavailability, thereby increasing the benefit risk ratio of drugs. Initially, only pressurized metered dose inhalers (pMDI) were available. However, pMDI require simultaneous actuation of the inhaler and inhalation, which appears difficult for many patients. Surveys suggest that pMDI are badly used by 14–90% of patients.[1–4]

This was an important reason for the develop-

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ment and introduction in the early 1990s of breath-actuated devices, including dry powder inhalers. The use of these devices seems to be easy or very easy in most clinical studies, with few inhalation errors. Evaluation of the handling of these new inhalers was mainly done shortly after giving instructions on use to selected patients. In real life, however, many errors seem to be made, but no wide-scale evaluation has been performed. The correct use of inhalation devices is essential to ensure the effectiveness of the treatment.[5] It has been recently demonstrated that inhaler misuse is associated with decreased asthma control in asthmatics treated with an inhaled corticosteroid.[6]

The aim of our observational study was to evaluate by general practitioners (GPs) in real life the handling by patients of their usual inhaler (Aerolizer®, Autohaler®, Diskus®, pMDI, or Turbuhaler®).

MATERIALS AND METHODS

GPs (n = 575) randomly selected based on their postal code number agreed to participate in a study assessing the handling by patients of their usual inhaler. A copy of the package leaflet of each inhaler was provided.

Physicians were asked not to give any instructions before the test and to pay attention particularly to the loading of the dose, to the way patients exhale with the dry powder inhaler, and to "smoke" escaping the pMDI.

Sampling

The GP had to complete at least four of nine standardized questionnaires (two for Aerolizer®, two for Autohaler®, two for Diskus®, one for pMDI, and two for Turbuhaler®). Consecutive patients were requested to take a puff of their usual inhaler with their usual inhalation technique, which was observed and rated by the GP.

Measures

In order to assess patient handling of their own inhaler device, a specific checklist of the key features of the inhalation technique (scored yes, no, don't know) was previously established for each inhaler model, from the package leaflet. These included opening the device, loading the dose, exhalation before inhalation, putting the device to mouth, inhaling deeply, and maintaining apnea for a few seconds. General questions were asked to the patient (perception of the drug, mouth discomfort) and to the GP (cough after inhalation, opinion of nasal inspiration, and complete dose inhalation).

Before returning the completed questionnaires, the GPs were asked their opinion on the study, if their participation taught them anything, how often they checked patient inhalation before the study, and how often they planned to check patient inhalation after their participation in the study.

Analyses

Errors were considered device independent if they corresponded to a lack of exhalation before inhalation or to patients not holding their breath a few seconds after inhalation. Other errors were considered device-dependent. Errors were considered critical if they could have substantially affected dose delivery to the lung. These critical errors were defined prior to the study by an expert committee and not revealed to the GPs before the study. They included lack of inhalation through the mouthpiece for all devices, canister in the wrong position for pressurized inhalers, blowing in the device before inhalation for dry powder inhalers, and, for the following:

1. Aerolizer®: Lack of capsule insertion, lack of two-button press and release
2. Autohaler®: Missing raising lever to vertical position
3. Diskus®: Missing sliding the lever as far as possible
4. pMDI: Lack of synchronization of hand actuation and breathing in
5. Turbuhaler®: Not holding inhaler upright for grip rotation[7] (tolerance ± 45°), missing rotating grip clockwise then counterclockwise until "click"

As we could not measure inhalation flow and duration in this real-life study, inhalation parameters were not included in critical error definition. Overestimation of the inhalation was defined as an estimation by the GP that the whole dose was inhaled, in the presence of at least one critical error. Descriptive analyses were done on each form, expressed as a percentage for qualita-

tive variables and as a median for quantitative variables. A significance level of 5% was adopted for statistical analyses. A polychotomous logistic regression model allowed the investigation of the weight of each error for the five inhaler devices simultaneously. The devices constituting the nominal categories of the dependent variable were adjusted for age in years and gender. Analyses were conducted using STATA software (STATA Corp. 7.0, College Station, TX) for logistic regression.

RESULTS

A total of 575 GPs participated in this study (116 women and 459 men, mean age 45.4 years) and returned 3,811 inhalation questionnaires (769 Aerolizer®, 728 Autohaler®, 894 Diskus®, 552 pMDI, 868 Turbuhaler®) between February 1st and July 14th, 2002. Patient characteristics are summarized in Table 1.

Main inhalation errors by device are described in Table 2. The two most common errors were failure to breathe out before actuation (28.9%) and not holding breath a few seconds (28.3%). These errors were considered as device-independent and observed in 40–47% of the patients. Although device-independent, small but statistically significant differences appear between devices. Their relevance is questionable.

Seventy-six percent of patients made at least one error with pMDI compared to 49–55% with breath-actuated inhalers (Table 3). Critical errors were made only by 11–12% of patients treated with Aerolizer®, Autohaler®, or Diskus® compared to 28% and 32% of patients treated with pMDI and Turbuhaler®, respectively. Overestimation of good inhalation by GPs was maximal for Turbuhaler® (24%) and lowest for Autohaler® or pMDI (6%). The frequency of critical errors increased with age for all devices (Fig. 1).

Responses to general questions confirmed after adjustment by inhaler content that β2 agonists were better perceived by patients and induced less coughing than corticosteroids. Corticosteroids also induced significantly more mouth discomfort (Table 4).

More than 90% of the GPs declared that participating in the study helped them recognize and identify errors, and over 93% declared that they would check their patients' inhalation technique more often. GPs estimated that they checked inhalation technique in four out of 10 patients before the study. They declared their intention to check inhaler technique in nine out of 10 patients after the study.

DISCUSSION

This study is the first large observational comparison of the handling by patients of the main inhalation devices, in real life in primary care. It confirms previous studies performed with pMDI showing that fewer than 25% of patients are able to inhale through pMDIs properly.[3] The number of patients making at least one error with breath-actuated inhalers is also high in our study, with less than 50% of patients inhaling correctly. There is little difference between breath-actuated inhalers for device-independent errors. When looking at de-

TABLE 1. PATIENT CHARACTERISTICS

	Aerolizer	*Autohaler*	*Diskus*	*PMDI*	*Turbuhaler*	*Total*
Number of patients	769	728	894	552	868	3811
Male/female (%)	54/46	53/46	51/49	54/46	52/48	53/47
Age, mean (years) ± SD	50 ± 20	47 ± 21	50 ± 21	47 ± 21	48 ± 21	49 ± 21
Age distribution (%)						
≤30 years	19.4	27.8	21.7	29.3	25.7	24.4
31 to 65 years	53	46.6	47.6	42.2	45.8	47.3
≥65 years	27.6	25.7	30.7	28.6	28.6	28.3
Disease						
Asthma (%)	72	70.1	68.6	75.6	68.1	70.5
COPD (%)	26.1	25.2	28.3	21.1	27.9	26.1
Active drug inhaled for the test						
Short-acting β2	/	298	/	376	210	884
Corticosteroids	/	442	175	109	411	1,117
Long-acting β2	755	/	170	40	/	965
Corticosteroids + long-acting β2	/	/	543	12	231	786

TABLE 2. PERCENT PATIENTS WHO WERE SCORED "NO" TO KEY FEATURES OF THE INHALATION TECHNIQUE CHECKLIST BY INHALER

	Aerolizer (*n* = 769), %	*Autohaler* (*n* = 728), %	*Diskus* (*n* = 894), %	*PMID* (*n* = 552), %	*Turbuhaler* (*n* = 868), %
Shake the inhaler				33.5	
Insert capsule[b]	0.7				
Press and release the 2 buttons[b]	3.8				
Raise lever to vertical position[b]		6.2			
Hold mouthpiece towards them			7		
Slide the lever as far as possible[b]			2.5		
Hold inhaler upright (tolerance of ±45°)[b]					18.1
Rotate grip and back until "click"[b]					14.9
Exhale before inhalation[a]	32.8	22.3	29.5	30.4	29.5
Exhale away from mouthpiece[b]	6.9		6.6		5.3
Inhale slowly and press canister[b]				25.5	
Press canister only once per inhalation[b]				31	
Inhale through the mouthpiece[b]	1.4		1.9		0.9
Inhale through the mouthpiece inhaler held correctly[b]		5.4		5.5	
Continue slow and deep inhalation after puff release		36.9		37.2	
Hold breath a few seconds[a]	28.4	30.2	26.4	31	25.4

[a]Device-independent item.
[b]Considered "critical error" if quoted "no."

vice-dependent errors, there are clear differences between inhalers, with Aerolizer® and Diskus® being the better used devices. Because some of the errors may be of little clinical significance, we had defined as critical errors those that could significantly affect drug disposition to the lungs. About one-third of patients regularly treated with pMDI or Turbuhaler® made critical errors. These were mainly, for Turbuhaler®, incorrect loading of the dose and blowing in the device and, for pMDI, the lack of hand–lung synchronization.

Aerolizer®, was according to GP opinion, the device that was the most frequently associated with the inhalation of the whole dose. This may be explained by the ability offered by this device to check the inhalation by looking at the empty capsule.

Our study differs from clinical trials comparing treatments. In these studies, one of the inclusion criteria is the ability of patients to correctly use the devices tested, and particular attention is given to patient education. The results of these controlled studies may therefore not be fully transposable to real life.[8–11] It is almost impossible to predict in a trial all the errors that patients will make with their inhaler device. Therefore, studies comparing in real life how the treatments are inhaled are clearly needed and complementary to controlled trials of inhaled treatment efficacy, since the results of the

TABLE 3. ERROR SUMMARY BY SYSTEM

	Aerolizer (*n* = 769), %	*Autohaler* (*n* = 728), %	*Diskus* (*n* = 894), %	*PMID* (*n* = 552), %	*Turbuhaler* (*n* = 868), %
At least one error	54 [50–57]	55* [52–59]	49 [46–53]	76* [73–80]	54* [51–58]
At least one device-dependent error	12 [10–14]	41* [38–50]	16* [14–19]	69* [66–73]	32* [29–35]
At least one critical error	12 [10–14]	11 [9–14]	11 [9–13]	28* [24–32]	32* [29–35]
GPs opinion (patient inhaled the right dose)	80 [77–83]	66* [62–69]	758 [72–77]	50* [46–54]	70* [67–73]
Overestimation by GPs	11* [8–13]	6 [4–8]	9* [7–11]	6 [3–9]	24* [21–28]

*$p < 0.05$ compared to the best result adjusted by age and gender.
Results are mean % [IC 95%].

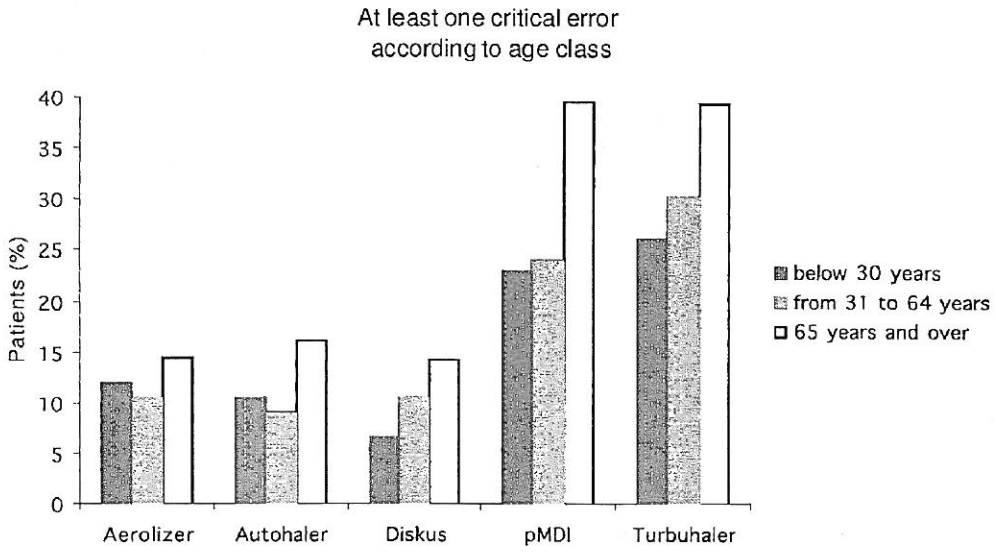

FIG. 1. Frequency of critical errors by device according to age class.

trials will apply only at best to that fraction of the patients who actually use their device properly.

The confidence of the GP in the inhalation device was estimated by the overestimation of correct inhalation (estimation by GP of correct inhalation in the presence of a critical error). The overestimation for pMDI was among the lowest. This may be due to intensive education on pMDI misuse, in consequence of which practitioners are able to identify errors. On the other hand, the proper use of the Turbuhaler® was often overestimated. This may be due to the lack of education on how to check for good inhalation. Educational efforts are clearly needed to inform GPs about errors in loading the dose.

GPs were not specifically trained to detect inhaler misuse. We have not been able to measure the inhalation parameters in this real-life study, and therefore the definition of critical error we have considered is likely to underestimate all errors that may significantly affect drug delivery. The frequency with which inhaler technique was observed to be correct was a function of, not only the skills of the patient, but also of the observing GPs. Therefore, the specified percentage of patients with errors is likely not to be accurate. However, assuming that this error in assessment applied equally to all devices, the relationship between devices would still be preserved. Under-diagnosis of inhaler misuse is more likely to characterize this study. This is confirmed by the discrepancy between the GP's opinion on the inhalation of the whole dose and the presence of a critical error. Blowing in a powder device and errors in loading the dose may not be perceived by GP as critical, depending on the device. Beyond the assessment of device use by the patients, this study may have modified the GP's perception and

TABLE 4. DRUG PERCEPTION AND SYMPTOMS ACCORDING TO THE ACTIVE DRUG AND THE DEVICE TESTED

	Aerolizer	*Autohaler*	*Diskus*	*pMDI*	*Turbuhaler*
Perception of the drug (%)					
Short-acting β2	—	61.7	—	73	52.2
Corticosteroids	—	55.7	57.5	71.6	39
Long-acting β2	64.3	—	55.3	62.5	—
Corticosteroids + long-acting β2	—	—	56	83.3	43
Cough (%)					
Short-acting β2	—	14.8	—	15.2	9.5
Corticosteroids	—	18.8	11.5	22	11.4
Long-acting β2	14.3	—	14.1	25	—
Corticosteroids + long-acting β2	—	—	15	16.7	10.4
Mouth discomfort (%)					
Short-acting β2	—	13.2	—	15.9	12.1
Corticosteroids	—	14.1	14.9	26.2	18.2
Long-acting β2	10.8	—	11.8	17.5	—
Corticosteroids + long-acting β2	—	—	16.3	33.3	15.7

awareness of inhalation errors: most GPs stated that they had learnt something and would be more attentive to patient inhalation technique in the future. We are not sure how this may have modified their observation of user errors during this short study.

We did show that, overall, GPs felt they had learnt from the study. There is room for improvement in training in the use of inhalation devices for patients and for GPs. We did not, however, reach all GPs. Further education on this topic seems needed to improve the quality of the management of bronchial diseases, an increasing burden to health care.[12]

CONCLUSION

Despite an improvement of inhalation technique with breath-actuated inhalers, patients still make a number of errors, some of which are critical to the efficacy of the inhaled treatment. The breath-actuated inhalers are not equal in real life in the frequency of device-dependent errors and critical errors. Therefore, the equivalence of efficacy demonstrated in controlled trials is unlikely to be transposable to real life. This may be due in part to the lack of communication by pharmaceutical companies about errors that can be made with their own devices and the lack of the possibility of easily detecting an inhalation error. More transparency would be of benefit to the education of GPs and patients, and may subsequently improve the efficacy of the treatments. Pharmaco-epidemiological studies comparing treatment efficacy in real life is complementary to controlled trials. They are especially needed for inhaled treatments, as inhalation errors are not measured in controlled studies when proper use is an inclusion criterion.

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