Evaluation of the effectiveness of four different inhalers in patients with chronic obstructive pulmonary disease

J van der Palen, J J Klein, A H M Kerkhoff, C L A van Herwaarden

Abstract

***Background* – The percentage of patients inhaling their medication effectively varies widely, according to methods of assessment and inhalers used. This study was carried out to assess differences among four types of inhalers using inhaler-specific checklists.**

***Methods* – Inhalation technique was evaluated in adult patients with chronic obstructive pulmonary disease (COPD). Inhalers investigated were either metered dose inhalers (MDIs) or the dry powder inhalers Turbohaler (Turbuhaler), Diskhaler, and Rotahaler. Errors were recorded against inhaler-specific checklists. From these, scores were derived by dividing the number of items correctly completed by the total number of items on the checklist and the result was expressed as a percentage. For every inhaler "essential actions" were identified and scores on these key manoeuvres were calculated. The percentage of patients performing all these essential actions correctly was also calculated. Scores were also compared with adjustment for differences in relevant patient characteristics.**

***Results* – Important differences among inhalers were found. Of 152 patients with COPD (mean (SD) age 55·1 (8·7) years), those with MDIs performed worst, especially when only essential items were considered. Patients with a Diskhaler did best, although after correction for patient characteristics the differences tended to diminish. Only 60% of patients were able to perform all essential inhaler actions satisfactorily. Of those using the Diskhaler, 96% did so correctly, while the corresponding figure for those using the MDI was only 24%.**

***Conclusions* – Many patients with COPD use their inhaler ineffectively. After adjusting for patient characteristics, differences among inhalers, although less pronounced, persist. Patients using a Diskhaler made fewest errors, while most patients using MDIs made crucial mistakes.**

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Inhaled medication plays an important part in the treatment of asthma and chronic obstructive pulmonary disease (COPD). In the Netherlands two types of inhaler are in common use: metered dose inhalers (MDIs) and (in the majority) dry powder inhalers (DPIs). Both have their advantages and disadvantages. MDIs are small, easy to carry, and deliver at least 100 doses, but they require good hand-lung coordination to achieve the best results.[1] DPIs, being breath actuated, are unaffected by hand-lung coordination, but patients need an inspiratory flow of more than 30 l/minute which might prove difficult to achieve for patients with severe COPD.

The percentage of patients inhaling their medication effectively varies from 2% to 85% according to the method of assessment and the type of inhaler.[2–11] A previous survey of inhalation technique in 123 patients with COPD[12] revealed that one third failed to use their inhaler effectively, and that inhaler-specific design features contributed significantly to the failure rate. The latter finding is confirmed in a number of other reports.[13–15]

To our knowledge, no comparable study of inhaler technique has considered such patient variables as age, sex, educational achievement, type of health care insurance, duration of disease, previous experience with the inhaler, or instruction in inhalation technique, all of which may influence the efficacy of treatment. In two studies an attempt was made to obviate these difficulties by means of a crossover design, but in both the patient sample was small (32 and 36 subjects) and the duration of follow up limited one and two months, respectively.[13 15]

This paper assesses differences among four different inhalation devices in relation to patient characteristics in a large sample of patients who have been using medication for a long time.

Methods

All patients with COPD aged between 18 and 65 years who attended the pulmonary outpatient department between February and June 1994 were included in the study. Those who had used inhaled medication for less than one month or with a limited ability to understand and speak Dutch were excluded. The remainder, a total of 152 individuals, formed the sample from whom the results were obtained. The inhalers investigated were MDIs and three dry powder devices (Turbohaler (Turbuhaler), Diskhaler, and Rotahaler). Other inhalers (for example, Autohaler, Spinhaler) and large volume spacers are seldom used in our department and therefore were not included in the study.

Table 1 Inhaler-specific checklists with items scores

		Item score (%)†
MDI checklist (n=25)		
(1)	Shake the inhaler‡	60
(2)	Hold inhaler upright	100
(3)	Exhale to residual volume	40
(4)	Keep head upright or slightly tilted	92
(5)	Mouthpiece between teeth and lips	68
(6)	Inhale slowly and press canister‡	48
(7)	Continue slow and deep inhalation‡	68
(8)	Hold breath for five seconds	44
Diskhaler checklist (n=27)		
(1)	Perforate blister‡	96
(2)	Exhale to residual volume	56
(3)	Exhale away from mouthpiece	78
(4)	Mouthpiece between teeth and lips	96
(5)	Inhale forcefully and deeply‡	100
(6)	Hold breath for five seconds	63
(7)	Exhale away from mouthpiece	89
(8)	Rotate disc	82
Rotahaler checklist (n=68)		
(1)	Keep Rotahaler upright‡	63
(2)	Insert Rotacap with transparent end down	96
(3)	Keep Rotahaler horizontal	85
(4)	Rotate both ends to open capsule‡	100
(5)	Exhale to residual volume	34
(6)	Exhale away from mouthpiece	56
(7)	Mouthpiece between teeth and lips	79
(8)	Inhale forcefully and deeply‡	90
(9)	Hold breath for five seconds	46
(10)	Exhale away from mouthpiece	79
Turbohaler checklist (n=32)		
(1)	Keep inhaler upright‡	69
(2)	Rotate grip anticlockwise and back until "click"‡	100
(3)	Exhale to residual volume	34
(4)	Exhale away from mouthpiece	50
(5)	Mouthpiece between teeth and lips	72
(6)	Inhale forcefully and deeply‡	94
(7)	Hold breath for five seconds	59
(8)	Exhale away from mouthpiece	84

† Percentage of patients performing the checklist item correctly.
‡ Essential checklist items.

Some patients were using more than one inhaler; in these cases the study was confined to one device only. The distribution within the patient sample was not uniform so, in order to redress the balance, a descending order of preference was established as follows: MDI, Diskhaler, Turbohaler, and Rotahaler. All inhalers were used regularly.

Twelve well trained lung function technicians performed all assessments of inhalation technique, using an inhaler-specific checklist specially developed for the purpose (table 1). The checklists were adapted from those issued by the Dutch Asthma Foundation and were tested in a pilot study, the results of which have been reported elsewhere.[12] Each patient was assessed by one lung function technician only. Disease and inhaler variables were similarly assessed by means of a checklist (table 2).

For each inhaler certain items are essential for optimal delivery of the active drug into the lungs. When errors are made regarding these key actions, it is likely that no or only an insignificant amount of medicine will be inhaled. These essential manoeuvres are different for the four types of inhalers.

MDIs must be shaken before use in order to mix the drug with the propellant (item 1, table 1). The patient should inhale slowly (less than $\pm$ 30 l/min) while simultaneously activating the canister (item 6); they should continue to inhale slowly throughout discharge (item 7).

In order to use the Diskhaler effectively it is necessary to perforate the blister completely (item 1) and to inhale the powder with sufficient inspiratory effort (item 5).

The Rotahaler must be held at an angle of less than 45° from the vertical while inserting the capsule (item 1). Otherwise, after opening the capsule (item 4), the drug may remain retained in the opening in the back of the inhaler. Patients are then often unable to generate enough inspiratory force (item 8) to inhale the powder. The presence of powder was checked by opening the Rotahaler after the demonstration by the patient.

The Turbohaler should also be held more or less vertically (item 1) while rotating the grip (item 2) to release the powder for a forceful inhalation (item 6).

Educational achievement was divided into less than (low) or more than (high) 11 years of schooling. Similarly, for a history of COPD a cutoff point of 10 years was chosen, whereas years of experience with the inhaler was divided into less than or more than four years.

Approval for the proposed investigation was given by the hospital's ethical committee and patients gave informed consent.

STATISTICAL ANALYSIS

Three analyses are presented. The first is based on all checklist items (analysis 1), the second involves a subgroup of selected "essential" checklist items only (analysis 2), while the third analysis is based on the percentage of patients completing all essential items correctly (analysis 3). The percentage of patients correctly completing each item on the checklist was calculated for each of the inhalers (table 1).

The total score for each inhaler was calculated by dividing the number of items correctly completed by the total number of items

Table 2 Patient characteristics

	MDI	Diskhaler	Rotahaler	Turbohaler	Total	Non-participants
No. of patients	25 (16%)	27 (19%)	68 (45%)	32 (21%)	152	11
Age						
>55 years (p=0·001)*	18 (72)	13 (48)	44 (65)	11 (34)	86 (57)	6 (55)
≤55 years	7 (28)	14 (52)	24 (35)	21 (66)	66 (43)	5 (45)
Sex (p=NS)*						
Men	17 (68)	20 (74)	45 (66)	14 (44)	96 (63)	7 (64)
Women	8 (32)	7 (26)	23 (34)	18 (56)	56 (37)	4 (36)
Experience with inhaler						
<4 years (p<0·001)*	7 (28)	26 (96)	18 (27)	24 (75)	75 (49)	4 (36)
≥4 years	18 (72)	1 (4)	50 (73)	8 (25)	77 (51)	7 (64)
Previous instruction (p=0·001)*						
Yes	20 (80)	26 (96)	44 (65)	30 (94)	120 (79)	5 (83)
No	5 (20)	1 (4)	24 (35)	2 (6)	32 (21)	1 (17)

* χ^2 test.

Table 3 Inhaler performance

Inhaler	*No. (%) of patients*	*All items*		*Essential items only*	
		Unadjusted mean score†	*Adjusted mean score‡*	*Unadjusted mean score*	*Adjusted mean score*
MDI	25 (16)	65·0	58·5	58·7	61·7
Diskhaler	27 (18)	82·4	71·6	98·2	96·6
Rotahaler	68 (45)	72·8	68·2	84·3	88·3
Turbohaler	32 (21)	70·3	61·3	87·5	88·4
Total	152	72·7	65·7	83·2	85·4

† Score = percentage of checklist items performed correctly.
‡ Adjusted for educational achievement, type of health care insurance, history of COPD, experience with the inhaler, and previous instruction in inhalation technique.

on the checklist and the result was expressed as a percentage. A score for the "essential" checklist items was similarly arrived at for each patient, together with the percentage of patients completing all essential items on the list correctly.

Unadjusted differences in scores among the four inhalers were tested with the Kruskall-Wallis test. Pairwise comparisons of inhalers were made with Wilcoxon's rank sum test. Differences among inhalers regarding discrete variables such as age categories, sex, and educational achievement were tested using the χ^2 test or Fisher's exact test. Differences in scores among the four inhalers, adjusted for type of health care insurance, educational achievement, history of COPD, years of experience with the inhaler, and previous instruction in inhalation technique were assessed using multiple linear regression analyses. Similarly, adjusted differences in dichotomous variables (a perfect score on essential checklist items or otherwise) among the four inhalers were calculated using logistic regression analyses. The limit of statistical significance was set at $p = 0{\cdot}05$ (two sided). Analyses were performed using the statistical package SAS.[16]

Results

One hundred and sixty three patients were asked to participate in the study. Of these, 11 refused. There were no apparent differences between the data obtained from these non-participants and those obtained from the participants.

Inhalation technique was assessed in 152 patients with COPD of mean (SD) age 55·1 (8·7) years, with an average length of history of 15·3 years (range 0–62). They had been using their inhaler for an average of 5·1 years (range 1 month to 29 years). Table 2 summarises the patient characteristics. Most (86%) patients found their inhaler easy to use, irrespective of type and manufacturer.

ANALYSIS 1: ALL CHECKLIST ITEMS

Individual item scores for the inhalers are reproduced in table 1. Mean overall score, inhaler specific scores, and differences among inhalers based on all checklist items are presented in tables 3 and 4. The mean (SD) overall score for all items and all inhalers was 72·7 (19·2)%. The most frequent errors were "not exhaling to residual volume" and "not breath holding for five seconds".

The Diskhaler achieved the best unadjusted mean checklist score compared with the other inhalers (all $p<0{\cdot}05$). After adjustment for educational achievement, type of health insurance, duration of disease, years of experience with the inhaler, and previous instruction in inhalation technique there were some changes in the scores (tables 3 and 4), but the Diskhaler was still significantly better than the MDI (13·1%; 95% confidence interval (CI) 1·6% to 24·6%) and the Turbohaler (10·2%; 95% CI 0·3% to 20·2%), although its superiority over the Rotahaler was reduced to 3·4% (95% CI −7·1% to 14·0%).

Patients who had received previous instructions in inhalation technique had a 9% higher score than those who had not (linear regression analysis, $p<0{\cdot}05$ for the regression coefficient). Similarly, patients with a private health care insurance showed a higher ability to use an inhaler effectively than those with public health care insurance (+10%, $p<0{\cdot}05$).

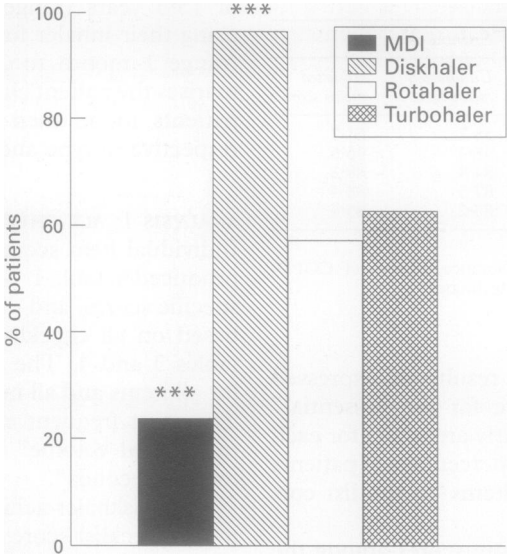
ANALYSIS 2: ESSENTIAL CHECKLIST ITEMS ONLY

Scores based on essential checklist items are reproduced in tables 3 and 4. Taking the unadjusted figures first, the mean percentage of manoeuvres performed correctly was 83·2%, and again there were significant differences between the inhalers. As before, the Diskhaler gave the best results (all $p<0{\cdot}005$) and the MDI the poorest (all $p<0{\cdot}001$). There was no significant difference between the Rotahaler and Turbohaler.

Table 4 Differences among inhalers

	All items		*Essential items only*	
	Unadjusted difference† (95% CI)	*Adjusted difference‡ (95% CI)*	*Unadjusted difference (95% CI)*	*Adjusted difference (95% CI)*
MDI *v* Turbohaler	−5·3% (−16·3 to 5·7)	−2·9% (−13·2 to 7·5)	−28·8% (−41·6 to 15·1)	−26·6% (−38·1 to −15·1)
Diskhaler *v* Turbohaler	+12·1% (2·0 to 22·2)	+10·2% (0·3 to 20·3)	+10·7% (3·4 to 17·8)	+8·2% (−2·9 to 19·3)
Rotahaler *v* Turbohaler	+2·5% (−5·4 to 10·4)	+6·8 (−2·1 to 15·7)	−3·2% (−11·1 to 4·7)	−0·1% (−10·0 to 9·8)
Diskhaler *v* MDI	+17·4% (6·9 to 27·9)	+13·1% (1·6 to 24·6)	+39·5% (26·9 to 51·9)	+34·8% (22·0 to 47·6)
Rotahaler *v* MDI	+7·8% (−0·7 to 16·3)	+9·7% (1·0 to 18·4)	+25·6% (14·9 to 36·3)	+26·5% (16·8 to 36·2)
Diskhaler *v* Rotahaler	+9·6% (1·7 to 17·5)	+3·4% (−7·1 to 14·0)	+13·9% (6·0 to 21·6)	+8·3% (−3·5 to 20·0)

† Wilcoxon rank sum test.
‡ Adjusted for educational achievement, type of health care insurance, history of COPD, experience with the inhaler, and previous instruction in inhalation technique (linear regression analysis).



*Percentage of patients performing all essential items correctly. *** Those using the MDI performed worse than those with any of the other three inhalers (all p<0·005). Patients using the Diskhaler performed better than those with any of the other three inhalers (all p<0·005).*

Adjusting for patient characteristics altered the results. Although the Diskhaler was still significantly better than the MDI (34·8%; 95% CI 22·0% to 47·6%), its superiority over both the Turbohaler (8·2%; 95% CI −2·9% to 19·3%) and the Rotahaler (8·3%; 95% CI −3·5% to 20·0%) was less marked.

For essential checklist items only the variables "previous instruction in inhalation technique" and "type of health care insurance" had no influence on the regression coefficients, but there was a tendency among patients who had been using their inhaler for more than four years to perform worse than those who had been using their inhaler for a shorter period (−7%, linear regression analysis, NS).

ANALYSIS 3: ALL ESSENTIAL CHECKLIST ITEMS CORRECT

Only 91 patients (59·9%) performed all key items correctly (figure). The percentage of those who did so with an MDI (24%) was significantly lower than for those using the other three inhalers (all p<0·005). Once again the Diskhaler gave the best results, 96·3% of patients achieving a 100% score on all key manoeuvres, significantly better than the other three devices (all p<0·005). There was no significant difference between the results for the Rotahaler and Turbohaler.

After adjustment for differences in patient characteristics, performance with the Diskhaler was still significantly better than with the others (p<0·05 for both the MDI and Turbohaler) but not for the Rotahaler (p = 0·06). The difference between patients using the MDI and the Turbohaler was not significant, while those using the Rotahaler or the Diskhaler did better than the MDI users (p<0·005 for both). There was no statistically significant difference between performances with the Rotahaler and the Turbohaler.

Discussion

How effectively did the patients in the study use their inhalers? A 72·7% success rate for all items on the checklist, rising to 83·2% when only essential actions are considered, suggests a generally acceptable inhalation technique. Only 60% of patients, however, succeeded in performing all essential manoeuvres correctly. When one or more errors regarding these key actions are made, significant amounts of medication may fail to reach the lungs.

In the present study the inhalation technique was evaluated subjectively by a trained lung function technician using an inhaler-specific checklist. Appel[11] has shown that a trained observer can achieve a 98% success rate in predicting a significant bronchodilator response from the subject's inhalation technique.

The performance of the inhalers differed considerably. Of those using the Diskhaler, 96% were able to perform all essential manoeuvres correctly while only 24% of those using the MDI managed to do so. Hilton reported an even worse performance for the MDI.[9] In his study the best performer was the Turbohaler, while in ours it was the Diskhaler. Hilton questioned the validity of his results, partly because of inequalities in the age distribution of his sample, and partly because of a suspicion that his scoring system may have favoured the Turbohaler.

The Netherlands differs from most other countries in that dry power inhalers are the most frequently prescribed form of inhaler therapy and there is no evidence that physicians prescribe specific inhalers based on patient characteristics making selection bias unlikely.

Our study examined whether patient variables could explain differences in checklist scores. Adjustment for education, type of health insurance, history of COPD, experience with the inhaler, and previous instruction did not alter the results much, although the differences tended to diminish.

In the patient group investigated, age, sex and education had no significant effect on the ability to use an inhaler correctly, although at 32–65 years (mean (SD) 55·1 (8·7) with a cut off at 65), the age range was somewhat narrow and may have influenced the results. In a previous survey of inhalation technique in 123 patients with COPD with a mean age of 63·7 years and no upper age limit, checklist scores were lower for all items (68%) and for key manoeuvres only (71%),[12] suggesting that the incidence of errors in inhalation technique does tend to increase with age. De Blaquiere *et al*[17] concluded that the patient's age and education had little influence on correct inhaler use, while Appel[11] found this to be true for age and sex. Appel also reported that older patients were less likely to learn to handle an inhaler successfully. De Blaquiere *et al* found that patients with the most experience with an inhaler produced the best results. Neither Appel's findings nor those of our study confirmed this conclusion. De Blaquiere *et al* also stated that patients who could recall having had additional instruction performed better. In our sample this was certainly reflected in the total checklist

scores but not when key manoeuvres only were considered. This could mean that patients remember the less important items and forget the essential ones, hence the need for stressing their relative importance.

As mentioned above, adjusting the figures to eliminate variations in patient characteristics did reduce the differences between the various inhaler scores but did not influence the overall result.

One aspect we did not investigate was the loading of the Diskhaler. Because manual dexterity is required, this might cause problems for some patients; this is also true for the Rotahaler. For patients with rheumatic arthritis, firing an MDI or twisting the Turbohaler grip might also prove difficult.

Although 79% of the patients had had some previous instruction in inhalation technique, 40% of patients performed some key actions incorrectly, and in consequence may have received little or no drug. This may result in prescribing of unnecessarily high doses and polypharmacy, generating higher drug costs and poorer asthma control.

We conclude that many patients with COPD use their inhaler ineffectively. After adjusting for patient characteristics, differences among inhalers, although less pronounced, persist. Fewest errors are made with a Diskhaler, while most patients using MDIs make crucial mistakes.

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