



## Early View

Original article

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# Comparison of inhalation technique with the Diskus® and Autohaler® in asthmatic children at home.

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## ABSTRACT

### Objective

Asthma is the most common chronic disease in childhood and anti-inflammatory medication is the cornerstone of treatment. Inhalers are frequently used incorrectly when demonstrated in the hospital, suggesting poor technique at home. We aimed to:

- 1) Compare daily inhalation technique with the Diskus® and Autohaler® in asthmatic children by filming inhalations at home;
- 2) Compare daily inhalation technique with technique demonstrated in the hospital.

### Methods

We performed a randomised study in asthmatic children (6-18 years) from the outpatient clinic of MST hospital from July 2014 to April 2016. Children received inhalation instructions for the Diskus® and Autohaler® and were randomised to use one device in the morning and the other in the evening. During the 28-days study period, inhalations were filmed at home and subsequently demonstrated in the hospital. All inhalations were checked for 7 critical errors per device.

### Results

A total of 636 videos with the Diskus® and 663 with the Autohaler® were provided by 27 children. The most common critical error in daily-life was an incorrect device position during preparation of the Diskus® (n=271) and an insufficiently deep inhalation (n=39) using the Autohaler®. Percentage of correct days using the Diskus® was 44%, compared to 96% with the Autohaler® (p<0.001). The two most common errors with the Diskus® were made at least twice as often at home than in the hospital.

### Conclusion

Inhalation technique at home was markedly better with the Autohaler® than with the Diskus®. Pediatricians should be aware that hospital-based demonstrations can overestimate daily inhalation technique with the Diskus®.

## INTRODUCTION

Asthma is the most common chronic disease in childhood. It is characterised by chronic airway inflammation and reversible airway obstruction with an increased airway responsiveness to a variety of stimuli (1). Daily anti-inflammatory medication is the cornerstone of treatment and can effectively reduce airway inflammation and control symptoms (2). The inhaled route is preferred as it minimizes systemic side effects while maintaining efficacy.

Commonly used devices for the inhalation of medication in childhood asthma are pressurised metered-dose inhalers (pMDI's) and dry powder inhalers (DPI's). Breath-actuated PMDI's such as the Autohaler® and Redihaler®, incorporate a mechanism activated during inhalation that triggers the metered-dose inhaler. In DPI's, such as the Diskus® and Turbuhaler®, the drug is dispersed into particles by inspiration (3).

Optimal pulmonary deposition of inhaled medication is highly dependent on a correct inhalation technique. Several studies have shown that inhalers are frequently used incorrect, leading to poor asthma control (4-7). A recent study conducted in a group of children hospitalized for asthma (7) found that almost half of their participants demonstrated improper inhaler use in the hospital. Kamps et al. (8) showed that comprehensive inhalation instructions are needed to attain a correct, hospital-observed, inhalation technique. Inhalation technique demonstrated in front of healthcare professionals may however overestimate daily technique at home. There are no studies yet focusing on the daily inhalation technique of children at home, which is vital information when attempting to improve asthma control. Therefore, we compared the daily inhalation technique with the Autohaler® and the Diskus® by filming inhalations at home and compared daily technique at home with technique as demonstrated in the hospital.

## METHODS

### Study design and patients

This study had a randomized design. From July 2014 to April 2016, children 6-18 years with a clinical history of asthma from the pediatric outpatient department of Medisch Spectrum Twente, Enschede, the Netherlands, were asked to participate. Patients were eligible when they already used inhaled steroids twice daily (using a non-breath actuated pMDI with spacer) or when their pediatrician was planning to start treatment with inhaled steroids.

### Study procedure

#### *Baseline visit*

At baseline visit, a medical history with a specific focus on asthmatic symptoms and a physical examination was carried out. Patients were randomly assigned to treatment group 1 or treatment group 2, using opaque sealed envelopes with a randomization number. Group 1 had to inhale one puff of fluticasone propionate 100 µg using the Diskus® in the morning and one puff beclomethasone dipropionate 100 µg with the Autohaler® in the evening, and group 2 *visa versa*. After this, patients were instructed on how to use the Diskus® and the Autohaler® by an experienced nurse practitioner, following standardized inhalation protocols of the Lung Alliance Netherlands (LAN) (9). Patients had to demonstrate a correct inhalation technique for both devices after receiving the instructions. This was also checked using the Inhalation Manager®, a computer-based measuring instrument which enables testing the entire inhalation manoeuvre of commonly used Breath Actuated Inhalers (10).

#### *Filming inhalation technique at home*

Over a study period of 28 days, patients or parents filmed the inhalation of their medication at home twice daily with an iPad® and were instructed to send the video clips at the end of each day. They were also instructed to inform the investigators when they experienced side effects. An electronic reminder was sent to the iPad® the next day if video clips were not received. Patients were excluded if video clips were not received more than three times in one of the four study weeks or more than three consecutive days. Video clips were scored according to a list of critical errors, partly adapted from the standardized inhalation protocols distributed by the LAN (9) (table 1). Critical errors were defined as errors that compromised the potential benefit of treatment, such as those that impede pulmonary drug deposition or delivery of a sufficient dose. All video clips were scored by the same investigator within 2 weeks after the last patient completed the study protocol.

#### *Follow-up visit*

At the end of the study period, patients visited the hospital for a live demonstration of their inhalation technique, performed in front of the same investigator that scored their inhalation videos, using the same list of critical errors (table 1).

### Statistical analyses

Results were expressed as mean values  $\pm$  standard deviation (SD) for the normally distributed continuous data and as median  $\pm$  interquartile range (IQR) for not-normally distributed data. Normality was tested by viewing normality plot and histograms. For nominal or ordinal data, numbers with corresponding percentages were used.

Differences in baseline characteristics between the study groups were tested with the Mann–Whitney *U*-test for the non-normally distributed variables and the independent *t*-test for the normally distributed variables. Differences between binary variables were tested with the Chi-square test or Fisher exact test as appropriate. The Wilcoxon Signed-Rank test was used to test the difference between the percentage of correct inhalations for both devices at home and for the median amounts of critical errors per device per patient. Time until the first critical error was analysed with the log-rank test and visualised with a Kaplan Meier plot. The McNemar test was used to analyse the percentages of patients that showed a correct inhalation technique during demonstration in the hospital.

A two-sided p-value of less than 0.05 was considered statistically significant. Data analyses and the random allocation sequence were performed with SPSS<sup>®</sup> Statistics, version 22.0.

### **Ethical considerations**

This study was approved by the Medical Ethics Review Board Twente and registered in the Dutch trial register (NTR, identification NL4302). All children and parents/guardians received written patient information and provided written informed consent before participating in the study.

## RESULTS

Of the 32 patients initially included in the study, 5 patients were excluded from further analyses because video clips were not received more than three times in one week or not received on more than three consecutive days. The 27 remaining patients provided a total of 1299 video clips; 636 with the Diskus® and 663 with the Autohaler®, which were all suitable for analyses.

### Characteristics of the study population

The baseline characteristics of the initial study sample (n=32) are shown in table 2. The initial study group comprised of 20 boys (62.5%) and 12 girls (37.5%) with a mean age of  $7.9 \pm 1.7$  years. After randomization, 16 patients were included in group 1 (Diskus® - Autohaler®) and 16 in group 2 (Autohaler® - Diskus®). No differences in baseline characteristics, but also not on inhalation technique at home or in the hospital between the groups were observed (table 2 and not shown). Accordingly, data are presented for the study group as a whole.

### Inhalation technique at home

During the study period of 28 days, a total of 451 critical errors were made with the Diskus®, compared to 63 errors with the Autohaler®. All patients made at least one critical error with the Diskus® during the study period, while 8 patients (29.6%) made no critical error using the Autohaler®.

The most common error with the Diskus® in daily-life was not holding the device horizontal with the counter facing up while preparing the dose before inhalation (n=271; 60% of errors with the Diskus®), followed by an insufficiently deep inhalation (n=83; 18%) and exhaling into the device (n=66; 15%) (table 3). The most common error using the Autohaler® was an insufficiently deep inhalation (n=39; 62% of errors with the Autohaler®), followed by an insufficient breath hold after inhalation (n=18; 29%).

With the Diskus®, the first error was made after a median of 2 [IQR 1-3] days, compared to 5 [IQR 4-14 days with the Autohaler® (p <0.001). Figure 1 shows the survival function of patients without a critical error during the study period, showing a more rapid decline when using the Diskus®.

The percentage of correct inhalations at home was 44% with the Diskus®, compared to 96% with the Autohaler® (p<0.001) (table 4). The median amount of critical errors made per patient was significantly higher using the Diskus® (14 [IQR 10-22]), compared to the Autohaler® (1 [IQR 0-20]) (p <0.001) (table 4).

### Inhalation technique in the hospital

During the demonstration in the hospital at the end of the study period, 19 children (70%) showed a correct inhalation technique with the Diskus®, and 23 children (85%) with the Autohaler® (p <0.001) (table 4).

In figure 2, the prevalence of the two most common critical errors for each device in the home situation and during demonstration in the hospital is presented. The two most common errors with the Diskus® (incorrect position of device and insufficiently deep inhalation) were made more than twice as frequent at home than in the hospital. The two most common errors with the Autohaler® (insufficiently deep inhalation and insufficient breath hold) were made slightly more frequent in the hospital than at home.

### Differences in age

Exploratory analysis were performed in two different age groups (6-7 years and 8-12 years old) (data not shown). Children in the younger age group made more errors compared to the older age group regarding deep inspiration and breath hold. This was observed for both

devices, although more pronounced in the Autohaler® group. In both age groups the demonstrated inhalation technique in the hospital with the Diskus® overestimated the daily technique at home.

## DISCUSSION

We found that the inhalation technique with the Autohaler® was well maintained after inhalation instructions, as in 96% of the study days no critical errors were made with this device. In contrast, we observed that the quality of medication administration with the Diskus® rapidly declined after receiving instructions. Worrysome, the daily technique with the Diskus® was not well reflected by demonstration in the hospital, overestimating the technique at home.

To our knowledge, this is the first study that investigated inhalation technique of asthmatic children by filming inhalations at home. Previous studies focused on inhalation technique demonstrated in a primary care or hospital setting, where technique was assessed through video conferencing (11) or directly in front of healthcare providers and caregivers.

Studies focusing on the inhalation technique of children using DPI's show a wide range of correct use. In a study by Sleath et al. (12), a correct Diskus® use was only found in 21.9% of the study population. Capanoglu et al. (5) found a correct use in 34.6% of their patients, comparable with the correct use of our study population at home. In a study by Malot et al. (13), primary care physicians assessed the inhalation technique of children with their current device using device-specific checklists. They found that 46% of their population made at least one mistake with the Diskus®.

Kamps et al. (8) observed a correct inhalation technique with the Diskus® in 79% of their study patients that had received instructions at a pharmacy, compared to 39% of the patients who had been trained by their general practitioner. In a control group that was trained at least twice by a research fellow during a six week period, 93% showed a correct technique. Similar to Kamps et al., we provided comprehensive inhalation instructions consisting of both information and training of inhalation technique. The difference in correct inhalation technique after receiving instructions between our study and the study by Kamps et al., could be due to the fact that the most common critical error in our study group was an incorrect positioning of the device during preparation; an error that was not taken into account in the aforementioned study. Also, the provision of repetitive inhalation instructions is likely to have had a positive effect on the sustainability of inhalation technique, as has been shown before by the same author (14).

The most prevalent critical error in daily life with the Diskus® was an incorrect preparation of the dose before inhalation; holding the device in a vertical position after opening the inhaler or holding the counter downwards. In the home situation this error was made during 42.5% of the inhalations. However, only 5 out of 27 children (18.5%) showed this error in the hospital during demonstration. Another common critical error at home with the Diskus® was not performing a deep inhalation (13.1%). Only 1 child showed this error in the hospital. Apparently children are less focused on a correct inhalation technique at home compared to a demonstration in the hospital in front of healthcare professionals. It is to be expected that the technique of children who do not participate in a clinical trial and are being filmed, is even less accurate. The risk of overestimating the inhalation technique with the Diskus® should therefore be taken into account by healthcare providers.

Technology-based methods for the monitoring of inhalation technique in general are promising. Several novel methods show good feasibility (11) and efficacy when it comes to maintaining a correct inhaler use (15). Sulaiman et al. (16) used a device that focused on both adherence and inhalation technique, monitoring most critical errors. Although efficacy on healthcare outcomes has not yet been proven (17), these novel methods could reduce the burden of hospital visits focusing on inhalation technique (15). There is a need for controlled studies investigating these new monitoring methods, focussing on both clinical outcomes and healthcare costs.



Although the Autohaler® is a commonly used device, we only found one other study focusing on the inhalation technique with this device in a pediatric population. In the aforementioned study by Malot et al. (13), 57% of the children made at least one error and 8% one critical error using the Autohaler®. Similar to our study, an insufficiently deep inhalation was scored as a critical error. However the second most frequent mistake in our population; an insufficient breath hold, was not scored as critical by Malot et al., making a comparison with our results difficult.

The two most common errors in our population were made slightly more frequent in the hospital than at home. Due to the overall low prevalence of errors with the Autohaler® however, this comparison is less powerful for this device.

A recent systematic review by Usmani et al. (18) showed a large variation in how critical inhalation errors are defined for different inhalation devices. For the Autohaler® as example, there is no consensus on whether to label an insufficient breath hold as critical or non-critical, and how long this breath-hold should be. The large variation in how inhalation errors are labelled makes it difficult to compare studies and to create a clear overview of the magnitude of the problem. We agree with Usmani et al. that there is need for a consensus on defining critical and non-critical errors.

In our study, we provided comprehensive inhalation instructions for the participants, based on a checklist with 7 critical errors, adapted from an inhalation checklist from the LAN (9) and based on our expert opinion. Children were only included if their technique for both devices was correct following instructions. This way, we tried to create the same correct baseline technique for both devices. The same nurse practitioner provided the inhalation technique training for all participants and scored the filmed inhalations and the hospital demonstrations.

A limitation of our study is that children used two devices simultaneously, which could have led to an increase in errors per device. On the other hand, it is plausible that by filming the inhalations at home the behaviour of the participants was positively influenced. We therefore suspect that in real life, inhalation technique for both devices will be worse than we showed in this study. As mentioned before, our checklist with critical errors was based on expert opinion and a widely used inhalation checklist in the Netherlands (14). Our list with critical errors was not validated, and therefore our choice of different errors can be subject for discussion.

Proper administration of inhaled medication is essential for effective asthma treatment. This includes a correct preparation of the dose before inhalation, especially with the Diskus®. Healthcare professionals should be aware of device-specific critical errors and should put emphasis on these possible errors during training of technique. We recommend the development of technological solutions focussing on the monitoring of inhalation technique and the provision of feedback in daily life, thereby hopefully reducing critical errors and optimising therapy.

In summary, inhalation technique at home was markedly better with the Autohaler® than with the Diskus® after receiving one inhalation instruction in the hospital. Healthcare professionals should be aware that hospital-based demonstrations can overestimate daily inhalation technique in children, but probably also in adults with asthma or COPD, especially when using the Diskus®.

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**Table 1.** List of critical errors used for the scoring of inhalation technique<sup>a</sup>

Critical error type	Diskus®	Autohaler®
	<i>Preparation</i>	
1	Device is not opened correctly until a 'click' is heard.	Inhaler cap is not removed before use.
2	Device is not held horizontal with counter facing up while preparing (45 degree tolerance).	Inhaler is not held upright with lever on top (45 degree tolerance).
3	Lever is not pushed back until another 'click' is heard.	Lever is not pushed up before inhalation.
<i>Inhalation</i>		
4	Exhales into the device.	After fully exhaling, teeth and lips are not sealed around mouthpiece
5	Mouthpiece is not correctly sealed between teeth and lips.	Inhalation stops directly after firing the inhaler.
6	Insufficiently deep inhalation.	Insufficiently deep inhalation.
7	No breath hold for at least 10 seconds.	No breath hold for at least 10 seconds.

<sup>a</sup>Partly adopted from the standardized inhalation protocols distributed by the LAN (7).

**Table 2.** Characteristics of the study sample at baseline (n=32)<sup>a</sup>

	Group 1 <sup>b</sup> (n=16)	Group 2 <sup>c</sup> (n=16)	Total (n=32)	p-value
Sex <sup>b</sup>				0.144
Female	8 (50%)	4 (25%)	12 (37.5%)	
Male	8 (50%)	12 (75%)	20 (62.5%)	
Age, years	8.0 (1.6)	7.8 (1.8)	7.9 (1.7)	0.977
Atopy <sup>b</sup>	14 (87.5%)	13 (81.3%)	27 (84.4%)	1.000
Medication use <sup>b</sup>				
SABA	14 (87.5%)	15 (93.8%)	29 (90.6%)	1.000
LABA	2 (12.5%)	2 (12.5%)	4 (12.5%)	1.000
ICS	11 (68.8%)	15 (93.8%)	26 (81.3%)	0.172
NCS	9 (56.3%)	5 (31.3%)	14 (43.8%)	0.143
LTRA	2 (12.5%)	2 (12.5%)	4 (12.5%)	1.000

<sup>a</sup>Categorical values are presented as n (%), age as mean (SD).

<sup>b</sup>Group 1: Diskus® use in the morning and Autohaler® in the evening.

<sup>c</sup>Group 2: Autohaler® use in the morning and Diskus® in the evening.

BMI: Body Mass Index (kg/m<sup>2</sup>). SABA: short-acting β<sub>2</sub>-agonist. LABA: long-acting β<sub>2</sub>-agonist.

ICS: inhaled corticosteroid. LTRA: leukotriene receptor antagonist. NCS: nasal corticosteroid.

**Table 3.** Prevalence of different critical errors with the Diskus® and Autohaler® at home (n=27)<sup>a</sup>

	Diskus®		Autohaler®	
<b>Critical error type<sup>b</sup></b>				
1	0	(0%)	0	(0%)
2	271	(60.1%)	4	(6.3%)
3	3	(0.7%)	0	(0%)
4	66	(14.6%)	1	(1.6%)
5	0	(0%)	1	(1.6%)
6	83	(18.4%)	39	(61.9%)
7	28	(6.2%)	18	(28.6%)
<b>Total</b>	<b>451</b>	<b>(100%)</b>	<b>63</b>	<b>(100%)</b>

<sup>a</sup>Analyses are based on 636 video clips with the Diskus® and 663 with the Autohaler®, made by 27 patients.

<sup>b</sup>For description of critical errors types, see table 1.

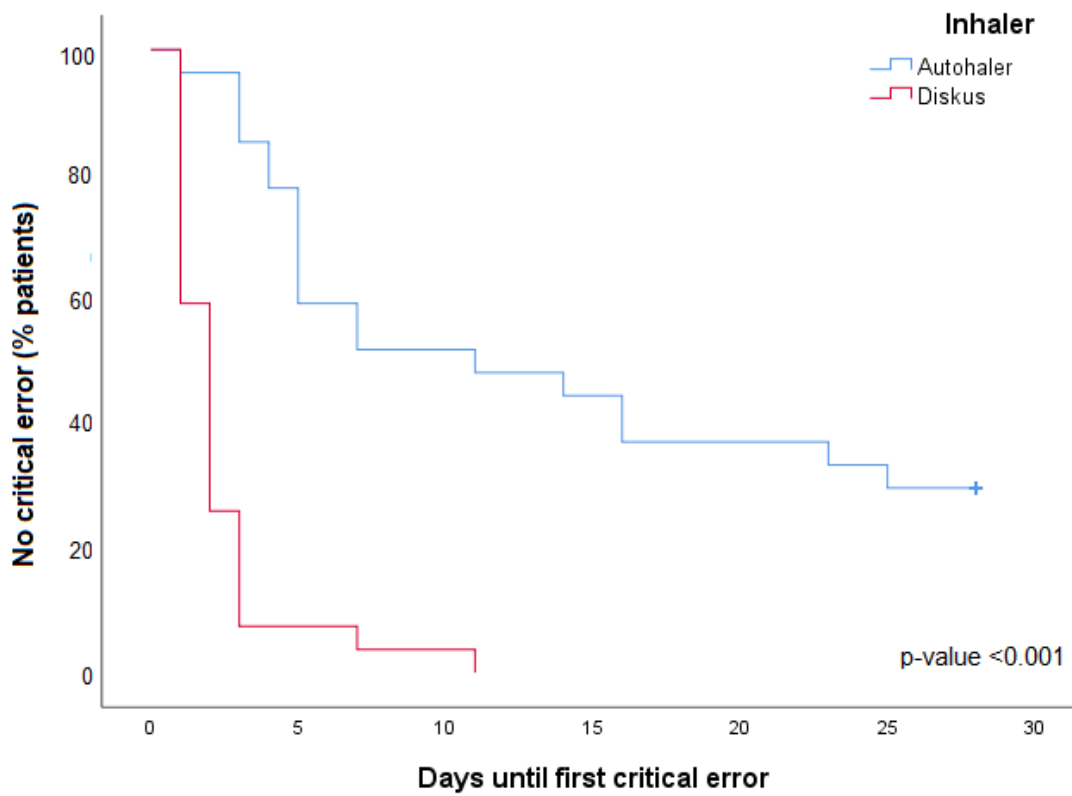
**Table 4.** Inhalation technique at home and during demonstration in the hospital with the Diskus® and Autohaler® (n=27)<sup>a</sup>

	Diskus®	Autohaler®	<i>p</i> -value
Median (IQR) percentage of correct inhalations at home <sup>b</sup>	44.0% (20.8-57.1)	95.8% (87.5-100)	<0.001
Median (IQR) number of critical errors per patient	14 (10-22)	1 (0-3)	<0.001
Correct inhalation technique in the hospital <sup>c</sup>	19 (70.4%)	23 (85.2%)	<0.001

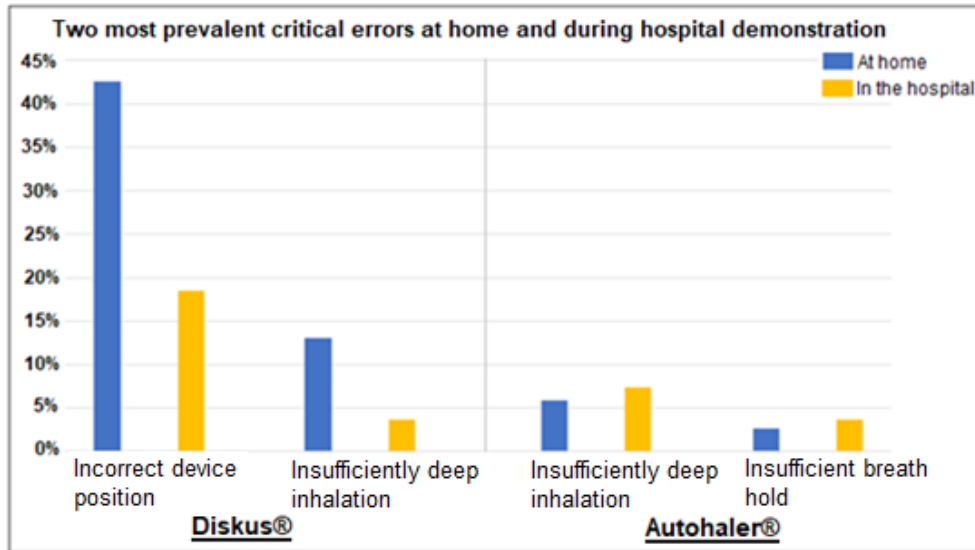
<sup>a</sup>Analyses are based on 636 video clips with the Diskus® and 663 with the Autohaler® made by 27 patients.

<sup>b</sup>Percentage of inhalations without a critical error.

<sup>c</sup>Patients that showed a correct inhalation technique during demonstration in the hospital at the end of the study period of 28 days, n(%).



**Figure 1.** Survival function of percentage of patients without a critical error during the study period of 28 days, using the Diskus® and Autohaler®.



**Figure 2.** Prevalence of the two most common critical errors at home using the Diskus® and Autohaler®, compared to the prevalence at demonstration in the hospital, expressed as percentage of total observations (n=636 for Diskus® at home; n=663 for Autohaler® at home, n=27 for both devices in the hospital).