



Wrong inhalation technique is associated to poor asthma clinical outcomes. Is there room for improvement?

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Purpose of the review

The long-term goals of asthma management are to control symptoms and to reduce the risk of exacerbations. Inhaled medication is the cornerstone of pharmacological treatment for asthma; therefore, good inhalation technique is the key for asthma management. However, up to 70% of asthma patients do not use their inhalers correctly. There is evidence on how poor inhalation technique is associated to poor asthma control. The purpose of this review is to present the most recent research in this field to help clinicians understand the importance of proper inhalers use and the possible interventions to optimize patients' inhalation technique.

Recent findings

New evidence on how poor inhaler technique and specific critical errors are significantly associated to poor asthma control and exacerbations and how this negative impact could be improved by optimizing device selection, enhancing shared decision-making and giving more importance to education, both for patients and healthcare professionals. New devices and additional tools might help patients to achieve the correct inhaler technique and could form the basis of simplified educational interventions.

Summary

There is an urgent need for specific interventions including new educational strategies to minimize the negative effects of wrong inhalation technique in asthma clinical outcomes.

Keywords

adherence, asthma, devices, disease control, education, inhalation technique

INTRODUCTION

Asthma is a chronic respiratory disorder characterized by symptom variability and episodes of acute worsening. Typical symptoms include wheeze, shortness of breath, chest tightness, and cough, together with variable expiratory airflow limitation. Given that 235 million people are reported to have asthma worldwide, this is an important global health problem [1]. The long-term goals of asthma management are to control symptoms and to reduce the risk of acute severe attacks (exacerbations). Asthma control should be assessed frequently, if possible using an appropriate questionnaire, as proposed by the Global Initiative for Asthma. Risk factors for exacerbations, loss of lung function, and medication side-effects should be avoided [1].

Asthma is mainly an inflammatory condition and anti-inflammatory treatment is the basis to maintain disease control. Despite the availability

of effective maintenance medication, most patients continue to use rescue short-acting beta agonists daily, indicating inappropriate medication use and/or inadequate control and approximately half of them continue to have uncontrolled asthma [2,3].

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KEY POINTS

- Asthma medications are delivered by inhalers that require specific complicated techniques to deliver the medication to the lungs. Despite the availability of effective inhaled medications that are equally effective if used correctly, many patients with asthma remain uncontrolled and suffer from exacerbations.
- Poor inhaler technique is a major cause of poor asthma control and exacerbations. Many critical errors have been identified with device use, but we should focus on those significantly associated with poor asthma outcomes.
- Device selection is crucial to get an adequate inhalation technique and many factors including patient's preferences and needs must be taken into account by prescribers to make the right choice.
- Education based on inhaler training can significantly improve asthma control. However, the evidence is of low quality and periodical intervention reinforcement and longer follow-up studies are recommended.
- New devices and technological improvements could help patients to learn the correct inhalation technique.

Inhalers are devices that deliver medication direct to the bronchial epithelium, facilitating the use of lower doses and reducing the risk of systemic side-effects. Devices range from pressured metered-dose inhalers (pMDIs) and spacers to soft mist and dry powder inhalers (DPIs), with each one working differently and requiring its own inhalation technique. Nebulizers could be also considered as a different inhalation device. Studies performed in controlled settings have shown that all inhaler types are equally capable of delivering appropriate medication doses [4] and meta-analyses have reported that all inhaler devices have comparable effectiveness if used correctly [5,6].

However, clinical experience has shown that asthma medications are less effective in daily practice than they are in clinical trials and ineffective inhalation technique could be related to poor asthma control. Each of the different drug delivery systems demands a certain level of physical skill, manipulation, dexterity, hand strength, lung capacity, and/or hand–lung coordination to ensure optimal/correct inhaler use. Taking these considerations into account, healthcare professionals could make the right choice to recommend a specific device. The device itself is at least equally as important as the prescribed drug and, in the future, the choice of drug compound might be considered of secondary importance [7].

Despite the established importance of good inhalation technique, many patients still do not use their inhalers correctly. A recent systematic

literature review and meta-analysis found, despite the large variability between studies, that incorrect technique was common across all devices, with error rates ranging from 50 to 100% and 14 to 92% for critical errors. Age, education status, previous inhaler instruction, comorbidities, and socioeconomic status have been associated with an increased frequency of handling errors [8^{••}]. Inhalation technique errors are unacceptably frequent, and, despite many interventions, they have not improved much over the past 40 years [9[•]]. Unexpectedly, the results among healthcare professionals did not either improved over time during the past decades and correct inhalation technique results were substantially worse than those from patients (15.5% for healthcare professionals vs. 31% for patients, respectively) [10[•]]. There is currently insufficient evidence to determine differences in error rates between different inhaler devices and their impact on clinical outcomes. Moreover, data are also needed from the newest easy-to-use inhalers [11].

Next to poor inhalation technique, adherence with inhaler therapy is also known to be poor among patients with asthma, with studies indicating that between 40 and 60% of patients are noncompliant [12]. Poor inhalation technique is considered the main cause for nonintentional adherence and it is easy to assume that poor compliance and poor inhaler technique are associated [13]. Careful instruction on inhaler technique may enhance adherence when the patients experience better outcomes.

During the past years, many studies have shown how poor inhalation technique is associated to poor asthma control and how specific measures could improve inhalation technique and asthma control and reduce exacerbations' risk. The purpose of this review is to present the most recent research in this field to help clinicians to understand the consequences of poor inhalation technique and therefore the importance of proper inhaler use. Specific devices' selection, inhalers' education, and technological advances both for inhalers and inhalation technique assessment are crucial to improve the management of asthma.

INHALATION TECHNIQUE AND POOR ASTHMA OUTCOMES

Studies have almost universally demonstrated an association between errors in inhalers use and poor asthma control with significantly higher rates of uncontrolled asthma among patients with incorrect inhaler techniques. Most of the available evidence is from cross-sectional studies. A summary of 18 recent studies specifically looking for an association between inhaler technique and asthma outcomes is

Table 1. Cross-sectional and interventional studies looking for association between inhaler technique and asthma outcomes

Reference	Country	Sample	Age	Inhaler device	Significant association between inhaler technique and
[14]	France	4.078	>15	pMDIs	AIS, exacerbation, resources
[15]	France	4.362	>18	pMDIs and DPIs	GINA control
[16]	Italy	699	>14	pMDIs and DPIs	ACT, hospitalizations, resources
[17]	Brazil	467	>18	pMDIs and DPIs	ACQ6
[18]	United Kingdom	3.981	All	pMDIs and DPIs	ACT, exacerbations, resources
[19]	Saudi Arabia	450	>18	pMDIs and DPIs	ACT
[20]	Spain	336	>18	DPIs	ACQ
[21]	Oman	218	>12	Not reported	ACT
[22]	Brazil	268	>18	pMDIs and DPIs	GINA control
[23]	Turkey	572	>18	pMDIs and DPIs	ACT
[24]	Portugal	62	>12	pMDIs and DPIs	ACT, CARAT
[25]	Turkey	171	<19	pMDIs and DPIs	GINA control, ACT
[26]	Jordan	130	>14	pMDIs and DPIs	ACT (no significant association)
[27 [•]]	Multinational	623	>16	DPI Diskus	GINA control, hospitalizations
[28]	India	330	>18	pMDIs	ACQ
[29 ^{••}]	Multinational	3.660	>16	pMDIs and DPIs	GINA control, exacerbation
[30]	Jordan	105	7–17	pMDIs	FEV1, ACQ, PAQLQ
[31]	Jordan	99	>14	DPIs	ACT

ACQ, Asthma Control Questionnaire; ACQ6, Asthma Control Questionnaire six questions; ACT, Asthma Control Test; AIS, Asthma Instability Score; CARAT, Control of Allergic Rhinitis and Asthma Test; DPIs, dry powder inhalers; FEV1, Forced Expiratory Volume in 1 s; GINA, Global Initiative for Asthma; PAQLQ, Pediatric Asthma Quality of Life Questionnaire; pMDIs, pressurized metered-dose inhalers.

shown in Table 1 table 1 [14–26,27[•],28,29^{••},30,31]. Only one of those studies found no association between errors and outcomes, but in that case, the sample was too small to conduct a sufficiently powered analysis [26].

Poor inhalation technique has not only been related to asthma control but also to other important health outcomes. Some of them have also looked for an association between inhalation technique and increased exacerbations, leading to unplanned health-care use and hospitalization [14,16,18,27[•],29^{••}]. In an analysis of 4000 patients with asthma in a UK database, significantly more patients with a history of one or more asthma exacerbations had poor initial inhalation technique compared with patients who had experienced no exacerbations [18]. Only one recent study has shown significant improvements in pulmonary function [30]. Just two studies were conducted in children (aged 1–19 years), also showing an association between wrong inhalation technique and poor asthma control [25,30].

The cost of asthma management is also considerable, and poor inhalation technique is a substantial contributor. Measures that can improve techniques, including easier-to-use inhalers or better patient and professional training, could not only improve disease outcomes but also lower treatment costs [32^{••}].

CRITICAL ERRORS

Specific devices are associated with specific errors that affect outcomes, and it is important to identify these if we are to develop meaningful interventions that can reduce the impact of poor technique on asthma outcomes. Not all errors have the same effect on asthma control and some of them could be considered as critical. A critical error has been defined as the one that may impact the effectiveness of the delivered drug and thereby lead to the sub-optimal disease control of asthma [33]. There is also evidence from ‘in-vitro’ experimental models that coordination and inspiratory flow rates could critically affect aerosol lung deposition from hydrofluoroalkanes metered-dose inhalers [34].

In a recent systematic review, the most common definition for a critical error among selected studies was an action affecting the lung deposition of the inhaled drug, resulting in little or no medicine reaching the lungs [8^{••}]. The Aerosol Drug Management Improvement Team consortium showed that 11–32% of patients make a key mistake that drastically reduces or prevents drug deposition in the lungs [35]. In a large cohort of 4078 patients with asthma, a subgroup of misusers (making at least one error or omission) was analyzed and coordination errors between actuation and inhalation on pMDIs

were shown to be associated to poorer asthma control. Stepwise analysis also indicated that some errors or omissions like holding pMDIs upside-down, lack of forced expiration before inhalation, inappropriate timing of device actuation, excessively high inspiratory flow rate, incomplete inspiration, double actuation, and failure to hold breath after inspiration independently correlated to asthma control. This was one of the first studies in which an inhalation error was considered critical [14].

The evaluation of critical errors was the rationale behind the implementing Helping Asthma in Real People (iHARP) database, an international initiative that includes questionnaire data from patients and healthcare providers in eight countries. Using this database, researchers conducted a historical, multinational, cross-sectional analysis (2011–2013) to identify the factors associated with serious inhaler technique errors, together with their prevalence, among 623 primary care patients with asthma who used the Diskus DPI. In total, 341 patients (55%) made at least one serious error. The most common errors were not related to the device itself: failure to exhale before inhalation (33%), insufficient breath-

hold at the end of inhalation (25%), inhalation not forceful from the start (21%), and hold inhaler in a downward position before drug inhalation (12%). The factors significantly associated with errors were asthma-related hospitalization in the previous year, poor asthma control in the previous 4 weeks, no inhaler technique review in the previous year, obesity, and female sex [27[■]].

The relative impact of each specific inhaler error on asthma control has been evaluated in the recently published ‘CRITical Inhaler misTakeS and Asthma control’ (CRITIKAL) study, also based on the iHARP database using data from 3660 asthma patients [29[■]]. In contrast to the previous study that only evaluated patients who used the Diskus device, [27[■]] or the one by Giraud *et al.* [14] that only evaluated patients using pMDIs, the CRITIKAL study included patients treated with various devices, including pMDIs, pMDIs and spacers, and two different DPIs (Turbuhaler and Diskus). Specific ‘critical’ errors were identified, defined as those significantly associated with poor asthma symptom control and exacerbations. Although these critical errors varied between devices, many were common to all devices (Table 2) [29[■]].

Table 2. Critical inhalation errors significantly associated to poor asthma outcomes

Critical error Significant association to	MDI		DPI (Turbuhaler)		DPI (Diskus)	
	OR for uncontrolled	OR for increase exacerbation rate	OR for uncontrolled	OR for increase exacerbation rate	OR for uncontrolled	OR for increase exacerbation rate
Did not remove cap, did not shake device before actuation	NS	NS	3.92 (1.20–12.90)	3.28 (1.52–7.07)	NS	NS
Dose compromised after preparation because of shaking or tipping	–	–	2.00 (1.27–3.16)	1.82 (1.16–2.85)	NS	NS
Not breathe out to empty lungs before inhalation	1.53 (1.08–2.15)	NS	1.20 (1.00–1.45)	NS	NS	NS
Did not have head tilted such that chin is slightly upward	1.38 (1.02–1.88)	NS	NS	NS	NS	NS
Did not seal lips around the mouthpiece	NS	NS	1.94 (1.13–13.85)	2.90 (1.84–4.60)	NS	NS
Exhale into the inhaler or not hold the inhaler upright	1.63 (1.07–2.50)	1.09 (0.70–1.70)	NS	NS	NS	NS
Actuation not correspond with inhalation or before inhalation	1.43 (1.04–1.98)	1.29 (0.91–1.84)	–	–	–	–
Inspiratory effort not slow and deep for MDIs	NS	NS	–	–	–	–
Insufficient inspiratory effort for DPIs	–	–	1.30 (1.09–1.54)	1.33 (1.07–1.64)	1.62 (1.23–2.14)	1.40 (1.07–1.82)
No breath-hold following inhalation (or holds breath for <3 s)	NS	NS	NS	NS	NS	NS
Incorrect second dose preparation, timing, or inhalation	1.35 (1.01–1.81)	0.91 (0.62–1.34)	NS	NS	NS	NS

OR is calculated after adjustment for all errors.

DPI, dry powder inhaler; MDI, metered-dose inhaler; OR, odds ratio.

Adapted with permission [29[■]].

In the systematic review by Usmani *et al.* [8¹¹], from 123 selected studies, up to 299 different critical errors in inhalation technique were described and checklists were often created by the authors themselves adding a huge variation. They conclude that a consensus definition for critical errors for each device is needed and they propose to classify individual errors into categories (e.g., inhalation maneuver, inhaler handling, device specific, generic, and so on) to make comparison and analysis simpler [8¹¹].

HOW TO IMPROVE INHALATION TECHNIQUE

Initiatives and interventions aimed at improving this situation have been used during the past 40 years. Although many and varied, they can basically be divided in three groups:

- (1) Improving device selection and enhancing shared decision-making.
- (2) Improving inhalation technique by educational interventions.
- (3) Improving inhalation technique through technological advances.

Device selection and shared decision-making

There are more than 200 drug-inhaler devices available [36] and choosing the right device for each individual patient is crucial to ensure correct technique and to improve the likelihood of good adherence to therapy. In the UK database analysis from Levy *et al.* [18], it was notable that patients receiving beclomethasone via a breath-actuated pMDI device and a spacer had better control than those receiving it via a pMDI without spacer (68 vs. 51%). Other studies have shown that the rate of incorrect use is higher for pMDI devices than for a breath-actuated pMDIs or DPIs, as they require more patient coordination and cognitive function. In a Turkish study, the rate of correct usage was 59% for DPIs and 31% for pMDI. The rate of correct usage increased to 93% for DPI and 45% for pMDI after training [37]. Devices vary widely with regard to technique, patient suitability, and patient preference, which make the role of the prescriber in selecting the optimal device potentially fraught and overwhelming. Moreover, patients have their own perceptions or preferences regarding inhaler choice, and these can influence treatment success. Device features such as simplicity, convenience, and overall experience are important to patients [11].

Most patients are prescribed with more than one inhaled medication introducing an additional

problem for prescribers. Several studies have shown that simultaneous use of different inhaler types is predictive of increased inhalation errors [38]. A large retrospective observational study of patients with asthma in primary care demonstrated that over 1 year after a first inhaled corticosteroid prescription, patients prescribed with the same device type for both controller and reliever therapy were significantly more likely to achieve better asthma outcomes than those prescribed mixed devices [39].

The situation can be further complicated by patients being switched between inhalers for therapeutic reasons, health insurance policies, or prescribing practices [13]. Furthermore, any change in device that is deemed necessary must be supported by strong training in new technique [40].

Although algorithms are available to aid device choice [41¹²], these tend to focus on inspiratory ability and basic physical traits, but they need to be supplemented with an in-depth understanding of adherence and technique behaviors in key patient subgroups. Shared decision-making can empower the patient, and it has been shown to improve both adherence and health outcomes. In a randomized controlled trial in which clinicians and patients negotiated a treatment plan that accommodated patient goals and preferences, shared decision-making was associated with a higher cumulative dose of medication over a one-year period, a higher likelihood of well controlled asthma, and better lung function [42].

Educational interventions

The lack of education and training for patients as well as professionals and the lack of repeated training could be important reasons for the continued high rates of incorrect inhaler technique. Although studies of different educational approaches have had different levels of success, education has been shown to be key factors to improve inhaled medication use. Two recent systematic reviews of published randomized controlled trials about inhaler education have been published. These systematic reviews have analyzed the evidence from before 2016 supporting the use of different methods of inhaler education. One systematic review includes 29 studies [43¹³] and the other one (also including chronic obstructive pulmonary disease) 39 [44]. The evidence is of low quality owing to important biases, the variety of interventions and measurement methods used, and to the imprecision in the estimates of effect. However, in general, studies that included clinically relevant endpoints mostly indicated favorable clinical effects. A summary of research about educational interventions and

Table 3. Interventional studies showing better asthma outcomes by improving inhaler technique 2015–2017

Reference	Country	Sample	Age	Inhaler device	Intervention	Duration	Main variable
[44]	Canada	441	>18	All	QACN learning program for educators	12 months	30-s asthma test
[45]	Serbia	231	>18	DPI (Turbuhaler)	Training in 7-step inhalation technique	3 months	GINA score and QoL
[46]	Portugal	44	>12	pMDIs and DPIs	Verbal instructions and physical demonstration	6–8 months	CARAT, PEF
[30]	Jordan	105	7–17	pMDIs	Trainhaler training device	6–8 weeks	ACQ, PAQLQ, PACQLQ
[31]	Jordan	99	>14	DPIs	Labels in device showing incorrect inhalation steps	3 months	ACT
[47]	Egypt	364	>18	pMDIs	Verbal counseling and trainhaler and Flo-Tone	3 months	PEF, FEV1/FVC

ACQ, Asthma Control Questionnaire; ACT, Asthma Control Test; CARAT, Control of Allergic Rhinitis and Asthma Test; DPI, dry powder inhaler; FEV1/FVC, forced expiratory volume in 1 s/forced vital capacity ratio; PACQLQ, Pediatric Asthma Caregivers Quality of Life Questionnaire; PAQLQ, Pediatric Asthma Quality of Life Questionnaire; PEF, peak expiratory flow; pMDIs, metered-dose inhalers; QACN, Qualified Australian College of Nurses; QoL, quality of life.

improvements in asthma outcomes published after 2016 is presented in Table 3 table 3 [30,31,45–48].

Both face-to-face and multimedia inhaler training improved patients' inhalation technique in most studies [43²²]. Educational interventions for inhaler technique were effective in the short term, but their effectiveness decreased over time when reinforcement or follow-up education was not given [44]. In many of the included studies, improvements in inhalation technique observed did not translate to any meaningful benefit for patient-important outcomes, such as exacerbations and quality of life [43²²]. Some interventions included the use of training devices to help patients understand and achieve a correct inhalation technique [18,30,48]. Key predictors for success were patient's initial technique and the time elapsed since the intervention. However, all patients benefited from education or training, regardless of the inhaler used, and neither the duration nor type of intervention (individual or group) affected outcomes [44]. Children may also benefit from interventions, but results tended to be less clear for children because fewer and smaller studies have included children [43²²].

Technological advances

Inhaler devices' designs are constantly changing and improving and devices to make inhalation easier have been usually tested. New devices are being developed that require fewer steps for correct inhalation. This leads to simpler educational interventions and less critical errors. Second-generation breath-actuated pMDIs reduce dependency on the patient's coordination of inhalation and actuation. Slow-moving soft mist inhalers have also introduced new characteristics to help inhalation technique to be effective in specific patients. Also, newly introduced DPIs offer

some improvements such as reducing the number of actuation steps or including dose protectors, which prevent release of the dose until sufficient flow rate is achieved. Electronic power-assisted DPIs (active DPIs) are currently in development [49]. A new generation of 'intelligent' pMDIs with electronic computation of dosage delivery is also being tested to compensate for inadequate adherence and to provide more reliable feedback on delivery [50]. Most of them are attached to an inhaler to identify and record the time and day of actuation that is automatically uploaded to a website and the most recent ones are also giving additional feedback on appropriate inhalation technique [51].

Technology can also be used as an educational tool. Many electronic devices that provide feedback on the accuracy of patient inhaler technique with a 'real-time' representation of the inhalation process are available. These devices could provide a more standardized method to educate patients about how to use their asthma inhalers in clinical settings by understanding the steps for a good technique [52²²,53]. There are specific devices for pMDIs, DPIs, or both. Some only assess the inspiratory flow rate, whereas others incorporate coordination for actuation of the aerosol canister and encouragement of long and deep inhalation. Ultimately, electronic monitoring devices used for adherence assessment could be also used to educate and train both patients and healthcare professionals alike [51]. In Table 4 table 4, we present a summary of the available electronic devices for inhalation technique assessment.

Web-based multimedia information systems could also be of help to train and mainly reinforce education in inhalation technique [53]. However, there is a lack of comparative research showing the best way to produce, present, and use these web-based materials.

Table 4. Electronic devices to assess inhalation technique for patients and healthcare professionals inhalation education

Name of the device	Inhaler compatibility	Main characteristics	“Real-time” feedback
2Tone Trainer	pMDIs	It trains to inhale at the correct speed (sound alarm) and helping coordination with no medication exposure	Yes
AIM	pMDIs and DPIs	Device screen shows different colored lights depending on the accuracy of inhalation coordination (pMDI), inspiratory flow, inhalation duration, and breath hold after inhalation	Yes
In-Check Dial	pMDIs and DPIs	It measures peak inspiratory flow and presents in a colored scale, helping to check if sufficient inspiratory flow for a specific device	Yes
Inhalation Manager	DPIs (Turbuhaler and Diskus) and BA pMDI (autohaler)	A computer-based measuring device that assesses the entire inspiratory maneuver and offers prediction of particles distribution in the lungs	Yes
INCA	DPI Diskus	Digital audio recordings are digitally stored and can be assessed by the provider and shown to the patient as an educational tool	No
Mag-Flo inhaler	DPIs (Turbuhaler, Diskus, Novolizer, handihaler)	It presents visual feedback about inhalation speed. The device is connected to the inhaler and it shows a green light when an optimum flow rate is reached	Yes
MDIlog	pMDIs	Printed information about list of inhalation events	No
pMDI datalogger	pMDIs	Audio information about the inhalation is presented in an excel file	No
Turbutest	DPI Turbuhaler	A replica connected to an electronic sensor measures and with a light system indicates if sufficient inspiratory flow and also if the rotation to prepare the dose has been correct	Yes
T-Haler	pMDIs	Interactive video game that shows the patient in a visual format whether the inhalation has been good enough in terms of inspiratory flow	Yes

AIM, aerosol inhalation monitor; BA pMDI, breath-activated pressured metered-dose inhaler; DPI, dry powder inhaler; INCA, INhaler Compliance Assessment; pMDI, pressured metered-dose inhaler.
Adapted with permission [52[■],53].

CONCLUSION

We have presented an overview of the most recent evidence about wrong inhalation technique and specific critical errors and poor asthma outcomes. The interventions and technological advances aiming to improve patients' inhalation technique have been also updated. However, there remain many unanswered questions related to inhaler use, including the solution to enable patients to develop proper technique, the optimal education and training methods, and the way to maintain good practice throughout life.

Qualitative research is especially needed, particularly focusing on the attitudes and preferences of patients receiving education about inhaler technique, the barriers to correct use, and the preferences for education. Coupled with this, qualitative evidence about healthcare professionals' experiences and attitudes about training patients with asthma could help to inform wider practice. Moving forward, it will be necessary to develop an optimal

education plan for the inhaler technique and to test it among patients with asthma. The role and the cost-effectiveness of electronic monitoring and feedback systems, used in combination with inhalers, are promising but need to be investigated in real-life settings.

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