

EXPERT REVIEW

THE SIGNIFICANCE OF INHALER TECHNIQUE & HOW TO IMPROVE IT

In this review piece, Professor David Price, Professor of Primary Care Respiratory Medicine, University of Aberdeen, describes a significant and long-standing unmet need for inhaler technique to be improved in patients with asthma and COPD, and sets forth strategies to achieve the sorely needed improvements.

INTRODUCTION

Respiratory care has evolved enormously over the last 50 years, but most of the issues faced by patients in terms of competent inhaler use have not changed at all. A number of critical drivers have had an impact on the growth of the respiratory care area, including: changes in treatment approach with a focus on health promotion rather than illness treatment and an emphasis on outpatient treatment rather than hospital admission; the increase in aging population with chronic respiratory disease; advancements in technology and patient demand for simple and user friendly devices; and health service economic constraints

Current treatment approaches for asthma and COPD comprise combination therapy with an inhaled corticosteroid (ICS) and long-acting beta agonist (LABA), which can be an effective solution for the control of symptoms and prevention of exacerbations for many patients.¹

Whilst it is known that correct use of inhalation devices is essential to ensure effective treatment. Many asthma and chronic obstructive pulmonary disease (COPD) patients remain undertreated as a consequence of poor inhaler technique.¹ Poor technique can impact drug delivery to the lungs leading to inadequate therapeutic benefit and increased risk for future asthma exacerbations. This in turn can lead to non-adherence² which has a significant impact on disease control in the asthma patient population and leads to increased economic burden.

At the recent Annual Meeting of European Respiratory Society (ERS), which took place in Munich, Germany on September 6-10, 2014, the symposium "Inhaler technique: human error or design challenge?," sponsored by Teva Pharmaceuticals, ignited debate on key issues such as under-treatment of asthma and COPD, the limitations of current inhaled therapies, and where the responsibility for good technique lies. Apart from the author, another discussant at the symposium was Professor

Helen Reddel of the Woolcock Institute of Medical Research (Sydney, Australia). Her four-step plan to improving asthma control led to a shift in focus on inhaler technique in the most recent Global Initiative for Asthma (GINA) guidelines.

ASSUME INHALER TECHNIQUE IS INCORRECT UNTIL PROVEN OTHERWISE

Numerous studies have found that despite many efficacious medicines, asthma control continues to be a problem for at least half the patient population, leading to frequent need of rescue medication, increased risk of exacerbations and limited activity.^{3,4}

- Poor asthma control leads to increased demand for urgent medical attention^{5,6,7}
- In both asthma and COPD, one or more critical errors in inhaler technique were associated with a 50% increase in the need for a corticosteroid course, hospital admission or emergency visit⁸
- Systematic assessments⁹ have found that 39% of patients have poor technique, 50% of them had poor technique and poor adherence
- Factors associated with poor technique include age, limited education, lack of training and prescription of multiple devices¹⁰
- Inhaler devices are complex and their use requires multiple steps
- Few HCPs can demonstrate correct use of inhalers^{11,12,13}

Before GINA 2014,¹⁴ many guidelines had given what may be perceived as an easier solution to poorly controlled asthma, there was a dependency on stepping up medication as a first step to control the condition.

A four-step plan to improve asthma control:

1. It may seem obvious but choose the most suitable device for the individual patient – it always helps as a healthcare professional to be able to use it yourself correctly without any instruction

Professor David Price

Professor of Primary Care
Respiratory Medicine
E: david@rirl.org
T: +44 1223 967 855
M: +44 7787 905 057

Academic Primary Care

Division of Applied Health Sciences
University of Aberdeen
Polwarth Building
Aberdeen
AB25 2ZD
United Kingdom

Research in Real Life (RiRL)

16 Raffles Quay
#33-03 Hong Leong Building
Singapore 048581

www.rirl.org

Inhaler	Critical Error
Metered dose inhalers (MDIs) without a spacer	Failure to remove cap
	Not holding inhaler upright
	Actuation not corresponding to inhalation; actuation before inhalation
	Actuation not corresponding to inhalation; actuation is too late (Puff 1)
	Failure to actuate
	Failure to inhale
	Inhale too fast
	Inhalation through the nose
Metered dose inhalers (MDIs) with a spacer	When asked, patient does not know how to tell that their device is empty
	Failure to ensure a tight seal when mouthpiece is inserted into spacer. There should be a click heard with the Volumatic and with the AeroChamber device. It should be inserted with tight seal and the inhaler should be vertical at 90
	Failure to hold spacer with inhaler upright
	Failure to actuate just one dose into the spacer (either no dose actuated or actuates more than one dose)
	Spacer mouthpiece is inserted correctly but failure to seal lips
	Failure to inhale through mouthpiece within two seconds of discharging one dose
	Failure to actuate a dose into the spacer
	Failure to inhale
	Inhalation through the nose
	Failure to hold breath (or to hold for <3 s)
	When using two doses, starting to inhale through mouthpiece within two seconds of discharging the first dose
	Coughing during the inhalation
	If prescribed Fostair (beclometasone + formoterol), failure to know that they should use their inhaler within 20 weeks/five months after receiving it from the pharmacy
	Spacer has faulty parts, valves, or cracks in the plastic
	Having washed the device in soapy/detergent water
Failure to air dry the device	
Failure to remove the cap	
Dry powdered inhalers (DPI): Diskus	Failure to slide cover as far as possible
	Failure to slide lever fully to open mouthpiece
	Holding in a downward position after dose preparation (before inhalation)
	Shaking after dose preparation
	Blowing into the device before inhalation
	Failure to put in mouth and seal lips around mouthpiece
	Inhalation is not forceful from the start
	Failure to inhale through mouthpiece
	Inhalation through the nose
Failure of the patient to know when the device is empty	
Dry powdered inhalers (DPI): Turbohaler	Failure to remove cap
	Shaking during preparation
	Device not held upright (mouthpiece skywards) when the base is twisted during dose preparation (within 45)
	Dose not prepared correctly twisting the base until it clicks
	Dose not prepared correctly turning it back to the original position
	Shaking after dose preparation
	Failure to put in mouth and seal lips around mouthpiece
	Inhalation is not as fast as the patient can achieve (defined as a very fast suck)
	Inhalation is not forceful from the start
	Failure to inhale through mouthpiece
	Inhalation through the nose
	Failure to breathe out slowly to empty the lungs
	Breathing out into the device before inhalation
	Failure to tilt head such that the chin is slightly upwards
	Inhalation is not as long as the patient can achieve
Failure to hold breath (or to hold for less than three seconds)	
Failure to replace cap after second inhalation	

Table 1: Summary of usage, handling and technique errors associated with four different inhalers / inhaler types.

2. Check technique at every opportunity – everyone in asthma care is responsible!
3. Use an effective mode of training – physical demonstration better than written instruction
4. Inhaler skills training must be repeated – for both patients and healthcare professionals.

Inhaler technique is an integral part of the GINA 2014 asthma management strategy. Instead of the usual step-up of medication when control is poor, checking of inhaler technique and adherence should take place first.¹⁴

It's critical we understand how inhalers work in real life since the patients we often see in consultations are not typically the ones who participate in clinical studies. As we see more inhaler errors, we also see more asthma instability⁵ – clearly this is an important association.

Several limitations of clinical research are important to note. There are systematic reviews that have even made their way into British asthma guidelines which say there are no differences between different inhaler devices! – this a result of all studies used being licensing studies for different devices. The entry criteria pose a challenge as, ethically, a study participant cannot be randomised to a device they cannot use, so patients are only randomised if they could manage the device(s) included in the trial, which obviously leads to equal outcomes.

THE DEVICE MATTERS

Regulatory clinical trials (RCTs) tend to focus on the drug, not the device. However, an old drug in a new improved inhaler might be better than a new drug in older, more complex inhalers. A device that is easy to teach and easy to maintain technique with can provide the best control over time.

WHAT SORT OF EVIDENCE DO WE NEED?

The Respiratory Effectiveness Group's review of existing evidence has demonstrated that current inclusion criteria for an average asthma trial are too restricted, e.g. lung function 50-80% predicted, 15% reversibility, perfect inhaler technique, non-smoker, no comorbidities, perfect adherence, still symptomatic, willing to fill in a diary twice a day, etc.¹⁵

Most patients do not have their technique checked as regularly in real life compared

with in a trial, enough normal ongoing care needs to be observed to understand truly how an inhaler can make a difference. Registration RCTs should not be used as part of a meta-analysis if we want to evaluate the association between inhaler technique and inhaler device and outcomes – alternatives such as longer-term Phase III trials or more pragmatic RCTs could be considered. A more pragmatic RCT will allow for broader inclusion criteria and a type of care that better reflect normal, real life.

Even this solution is still not a truly representative sample so there is a real need for “real life” data to complement this, for example, observational studies. In 13 years of guidelines, there has been no change to inhaler technique!

In the real world, patients usually use their inhalers incorrectly:

- 61% of patients are still getting their pMDI technique wrong even after three attempts¹⁶
- 90% of patients are making errors¹⁷
- 55% of people made at least one serious error with GSK's Diskus, often presented as the device associated with the least errors.

Another important point is that we healthcare professionals are not great at assessing technique. Frequently the reason we get it wrong is that we don't know how to use the device ourselves.¹⁸ Additionally, spacers are often provided as a lazy solution but still require education and training.

Presented at the ERS meeting, and published in *Respiratory Medicine*,¹⁹ Table 1 summarises handling and technique errors associated with different types of inhaler – MDIs without a spacer, MDIs with a spacer, the Diskus DPI, and AstraZeneca's Turbohaler DPI.

ELIOT STUDY

Continuing the theme that data about real-life inhaler technique is both different from and more relevant than information collected in RCTs, the 2014 ELIOT (Easy Low Instruction Over Time) study, sponsored by Teva, set out to explore how well patients maintain their technique.

- ELIOT is a novel, pragmatic, prospective trial which compares steps to mastery, and maintenance of mastery, for Spiromax[®] versus Turbohaler[®]
- A 12 week randomised, open-label, parallel group study which only included patients who have never used either device before
- The study better represents the real-

life scenario where patients go for many months between technique assessments

- This is an important and brave study as it's one of the few prospective randomised trials comparing different inhaler technique and different inhalers.

SUMMARY

Poor inhaler technique is widespread with the majority of patients making at least one critical error, and incorrect inhaler use is linked with uncontrolled asthma. Responsibility for ensuring correct technique lies with everyone in respiratory care. However, this also needs to be supported by innovation in inhaler design and technology. An optimal inhaler should be easy for a healthcare professional to teach and intuitive for a patient to use over an extended period of time. RCTs often focus on the drug inside, not the device itself which is just as important whereas real life and observational studies can provide a truer picture of how well inhalers really work and affect patient outcomes.

REFERENCES

1. Molimard M, Raberison C, Lignot S et al, “Assessment of handling of inhaler devices in real life: an observational study in 3811 patients in primary”. *J Aerosol Med*, 2003, Vol 16(3), pp 249-254.
2. McHorney C, “The Adherence Estimator: a brief, proximal screener for patient propensity to adhere to prescription medications for chronic disease”. *Curr Med Res Opin*, 2009, Vol 25, pp 215-238.
3. Rabe K, Adachi M, Lai C, Soriano J, Vermeire P, Weiss K, Weiss S, “Worldwide severity and control of asthma in children and adults: the global asthma insights and reality surveys”. *J Allergy Clin Immunol*, 2004, Vol 114(1), pp 40-47.
4. Murphy K, Meltzer E, Blaiss M, Nathan R, Stoloff S, Doherty D, “Asthma management and control in the United States: results of the 2009 Asthma Insight and Management survey”. *Allergy Asthma Proc*, 2012, Vol 33(1), pp 54-64 (doi: 10.2500/aap.2011.32.3518. Epub 2011 Dec 15.)
5. Giraud V, Roche N, “Misuse of corticosteroid metered-dose inhaler is associated with decreased asthma stability”. *Eur Respir J*, 2002, Vol 19(2), pp 246-251.
6. Lavorini F, Magnan A, Dubus J et al, “Effect of incorrect use of dry powder

- inhalers on management of patients with asthma and COPD*". *Resp Med*, 2008, No 102, pp 593-604.
7. Levy M, "Obtaining outcome data on asthma management: the UK National Review of Asthma Deaths". *Prim Care Respir J*, 2012, Vol 21(1), p 18. (doi: 10.4104/pcrj.2012.00017.)
 8. Melani A, Bonavia M, Cilenti V, Cinti C, Lodi M, Martucci P, Serra M, Scichilone N, Sestini P, Aliani M, Neri M, "Gruppo Educazionale Associazione Italiana Pneumologi Ospedalieri. Inhaler mishandling remains common in real life and is associated with reduced disease control". *Resp Med*, 2011, Vol 105(6), pp 930-938. (doi: 10.1016/j.rmed.2011.01.005. Epub 2011 Mar 2. Erratum in: *Resp Med*. 2012 May;106(5):757.)
 9. Crompton G, Barnes P, Broeders M, Corrigan C, Corbetta L, Dekhuijzen R, Dubus J, Magnan A, Massone F, Sanchis J, Viejo J, Voshaar T, "Aerosol Drug Management Improvement Team. The need to improve inhalation technique in Europe: a report from the Aerosol Drug Management Improvement Team". *Resp Med*, 2006, Vol 100(9), pp1479-1494. (Epub 2006 Feb 21. Review.)
 10. Sestini P, Cappiello V, Aliani M, Martucci P, Sena A, Vaghi A, Canessa P, Neri M, Melani A, "Associazione Italiana Pneumologi Ospedalieri Educational Group. Prescription bias and factors associated with improper use of inhalers". *J Aerosol Med*, 2006, Vol 19(2), pp 127-136.
 11. Guidry G, et al, "Incorrect use of metered dose inhalers by medical personnel". *Chest* 1992, Vol 101(1), pp 31-33.
 12. Chopra N, et al, "Does introduction of new "easy to use" inhalation devices improve medical personnel's knowledge of their proper use?" *Ann Allergy Asthma Immunol*, 2002, Vol 88(4), pp 395-400.
 13. Basheti A, et al. "User error with Diskus and Turbuhaler by asthma patients and pharmacists in Jordan and Australia". *Respir Care*, 2011, Vol 56(12), pp 1916-1923.
 14. *The Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA) 2014*. Available from: <http://www.ginasthma.org>.
 15. Roche N, Reddel H, Agusti A, Bateman E, Krishnan J, Martin R, Papi A, Postma D, Thomas M, Brusselle G, Israel E, Rand C, Chisholm A, Price D, "Respiratory Effectiveness Group. Integrating real-life studies in the global therapeutic research framework". *Lancet Respir Med*, 2013, Vol 1(10), pp 29-30. (doi: 10.1016/S2213-2600(13)70199-1. Epub 2013 Dec 2.)
 16. Haughney J, et al, "Choosing inhaler devices for people with asthma: current knowledge and outstanding research needs". *Resp Med*, 2010, Vol 104, pp 1237-1245.
 17. Price D, et al, "Assessment of potentially important device errors performed by asthma patients in the global iHARP review service". Abstract presented at IPCRG 2014
 18. Molimard M, Raberison C, Lignot S, Depont F, Abouelfath A, Moore N, "Assessment of handling of inhaler devices in real life: an observational study in 3811 patients in primary care". *J Aerosol Med*, 2003, Vol 16(3), pp 249-254.
 19. Price D, et al, "Inhaler competence in asthma: Common errors, barriers to use and recommended solutions". *Resp Med*, 2013, Vol 107(1), pp 37-46.

e^x pharma

4th

DRUG FORMULATION & BIOAVAILABILITY

Breakthrough Techniques in Optimizing the Screening, Delivery, Solubility, and Stability of Drugs and Biologics to Enhance Product Life Cycles

January 26-28, 2015 | Hilton Boston Logan Airport | Boston, MA

FOUR IN-DEPTH PROGRAM TRACKS FOCUSING ON THE NEWEST BIOAVAILABILITY ENHANCEMENT TECHNIQUES:

- Modeling & Simulation for Enabled Formulations
- Managing Formulation Evolution Throughout Drug Life Cycles
- Team Leadership Styles for Advanced Formulation Development
- Rethinking Early-Stage Formulation Methods

ALL-NEW CASE STUDIES:

- Agnostic modalities in future drug development
- Action plans to proceed without real human data
- Solid-state chemistry as the next focal point for drug design
- Latest challenges in simulating supersaturation
- Adjust to the shorter developmental timelines of fixed-dose combinations
- Optimal screening approaches for cocrystals
- Identify and address pH-dependent absorption
- Risk protocols for photoreactivity and phototoxicity
- Transition your teams from small to large molecule work
- Device-based oral biologic delivery

TO REGISTER / Call 866-207-6528 or visit www.exlevents.com/bioavailability