

Considerations when Selecting a Device for Asthma

a report by

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There are many highly efficacious medications and a range of delivery devices available today for the control and treatment of asthma. However, despite this range of options, management of asthma is still less than satisfactory for many people.¹ This is largely due to a combination of failure to take prescribed medications at the right time and failure to take them correctly. Delivery of therapeutics for asthma is typically via inhalation. There is a good history of using this route for asthma medications, even as far back as ancient Greek and Roman times. Inhaled aerosol medications have advantages over oral and parenteral routes as they allow for selective treatment of the lungs while reducing systemic adverse effects.² By and large, the benefits of aerosolized medications outweigh the drawbacks and, consequently, the National Asthma Education and Prevention Program (NAEPP) states that the major advantages of delivering drugs directly into the lungs via inhalation are that higher concentrations can be delivered more effectively to the airways and that systemic side effects are lessened.³ Furthermore, some drugs are therapeutically active only when inhaled (e.g. most corticosteroid preparations, cromolyn, and salmeterol). Manually operated squeeze nebulizers were developed in the early part of the 20th century, but devices that we would recognize today did not emerge until the middle of the century. In the 1950s, the Wright nebulizer was the precursor of the modern hand-held jet-venturi nebulizer; Riker Laboratories (now 3M Pharmaceuticals) developed the first pressurized metered-dose inhaler (pMDI) in 1956; and the 1960s saw the birth of the modern dry powder inhaler (DPI). Today, while nebulizers, MDIs, and DPIs are the mainstays of asthma treatment, there are many variants that require different inhalation techniques and timings on the part of the patient, and all of them have their unique benefits and drawbacks (see *Table 1*). This presents the physician with a confusing array of choice. This article will hopefully make the picture a little clearer.

Differences and Similarities Between Devices

The main types of inhalers are: nebulizers—jet and ultrasonic; pMDIs—chlorofluorocarbon (CFC; less common) or hydrofluoroalkane (HFA) propellant, breath-actuated or manually operated, and with or without

spacer/holding chamber, and DPIs. Ideally, an inhaler should be easy for a patient to use; it should also be easy for a physician to instruct a patient on its correct use. It should be portable and easy to inhale, regardless of the strength of the patient's inflow. It should also ensure that the correct amount of medication is delivered to the right part of the lungs, and reassure the patient that this had been done. The device should also report the number of remaining doses it holds. While a number of devices on the market currently come close—and are getting closer all the time—to this ideal, none are yet there.

Nebulizers

Jet, or compressed air, nebulizers function using the Bernoulli principle. Compressed gas passes through a small aperture into a larger volume. This reduction in pressure increases its velocity, and the gas picks up drug solution from a reservoir in droplets of around 15–500µm in size. These droplets hit baffles, producing smaller droplets, which are inhaled or returned to the reservoir. In contrast, ultrasonic nebulizers create sprays using a high-frequency ultrasonic signal (around 1–3MHz) generated by a piezoelectric transducer. While the newer ultrasonic technology allows such devices to be smaller, faster, and quieter, nebulizers are still, as a rule, larger and less portable than other types of inhalation device. They are also more time-consuming to use and require maintenance and cleaning. Furthermore, this type of delivery is inefficient and quite expensive per dose, although it does not require any co-ordination between inhalation and actuation. Consequently, nebulizers are reserved for use in emergency situations and for those patients unwilling or unable to use other devices, such as the very young and the very old.⁴

Metered-dose Inhalers—Press-and-breathe

More convenient for carrying around and for swift use, pMDIs are the most widely prescribed inhaler devices and can be used with the greatest variety of asthma therapies. The original MDIs developed more than 50 years ago used CFC for propellants, but since the Montreal Protocol these will be gradually replaced with other gases, such as HFAs. More than simply a stand-in for CFCs, pMDIs using HFAs deposit drug more efficiently in the lungs, have a less forceful impact on the back of the throat, and reduce the 'cold freon' upon inhalation, all of which are improvements over the old pMDIs.⁵ pMDIs deliver the drug in either solution or suspension that also contains a surfactant such as oleic acid or lecithin to reduce particle agglomeration.

Traditionally, the devices delivered the dose when the cylinder was pressed, meaning the patient had to co-ordinate his or her action and inhalation; this makes these devices difficult to use, particularly for



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younger patients.⁶ Furthermore, there are recommendations governing the inspiratory flow rate and holding of breath post-inhalation, both of which add to the difficulty of use. Adults, while typically more able to effectively co-ordinate their actions and hold their breath, can still make mistakes using a normal pMDI.⁷ To overcome some of these dexterity drawbacks, it is possible to fit a spacer or holding chamber to an MDI, which for a short while will retain the aerosolized suspension to be breathed in more normally. These have the additional benefit of reducing drug deposition in the oropharynx, thereby reducing the risk of local side effects such as oral candidiasis and dysphonia. On the downside, for the common plastic spacers, electrostatic forces cause particles to stick to the walls, which can considerably lower the amount of medication delivered to the lungs. Washing the spacer and letting it drip-dry can help with this, but does add a layer of complication to its use. Spacers need to be replaced when damaged or worn and should be checked every three to six months, further adding to the cost of treatment.⁸ There is a plethora of spacers on the market, all of which have different flow dynamics that affect the amount and size of the inhaled medication.

Metered-dose Inhalers—Breath-actuated

Breath-actuated pMDIs are another way of overcoming the difficulties of hand–lung co-ordination posed by press-and-breathe MDIs.⁹ Clinical studies have demonstrated that the use of the pirbuterol acetate breath-actuated inhaler (Maxair Autohaler™, Graceway Pharmaceuticals) is easy to teach,¹⁰ and delivers the drug to the lungs at least as well as a properly used conventional MDI and better than a poorly used conventional MDI,¹¹ and it helps reduce the number of prescriptions required per patient.¹² Moreover, it can be used effectively by patients with poor lung function¹³ and limited manual dexterity,¹⁴ as well as by the elderly.¹⁵ The majority of MDIs do not carry dose counters, making it difficult for the patient to know how much medication remains. One study of 50 consecutive patients attending a children’s asthma center found that nearly three-quarters did not know how many doses their device contained, and all used it until they could no longer ‘hear’ the medication when actuating. Furthermore, half did not shake the inhaler before use to evenly distribute the drug in the canister. All this means there is a risk that asthmatics will use their device for twice as long as intended, well beyond the time it is empty.¹⁶

Dry Powder Inhalers

DPIs are all breath-actuated and, unlike breath-actuated MDIs, rely on energy from the patient’s inhalation to create the small-particulate suspension. Therefore, DPIs do not contain propellants, making them not only more environmentally friendly than most MDIs, but also portable, durable, and easy to use; it is also easy to teach the technique. Like breath-actuated pMDIs or MDIs with spacers, DPIs do not require hand–lung co-ordination, but unlike those devices most do carry dose counters. DPIs keep the medication either in discrete dose units or in a reservoir. However, without the propellant, DPIs on average require a higher inspiratory flow to work. This makes them less suitable for younger patients or those with low levels of lung or cognitive functioning.⁶ DPIs can also lead to high levels of pharyngeal drug deposition.

Choosing Between the Different Devices

While there are obvious differences between and within the types of asthma inhalers, there is actually little evidence that they differ in terms

Table 1: Advantages and Disadvantages of Inhaled Medications

Advantages	Disadvantages
Direct treatment of lungs	Less than optimal technique decreases drug delivery and potentially reduces efficacy
<ul style="list-style-type: none"> • High drug concentrations in the airway • Reduced systemic adverse effects 	
Inhaled beta ₂ -agonist bronchodilators produce a more rapid onset of action than oral delivery	The proliferation of inhalation devices has resulted in a confusing number of choices
Some drugs are active only with delivery	Inhaler devices are less convenient than oral medications <ul style="list-style-type: none"> • Greater time required for drug administration • Some patients may find the device less portable
Painless and often convenient delivery	

Table 2: Delivery Devices and Available Medications

Drug	Delivery Device		
	MDI	DPI	Nebulizer
Beta-agonists			
Aformoterol (L)			✓
Albuterol (S)	✓		✓
Fenoterol (S)			
Formoterol (L)		✓	
Levalbuterol (S)		✓	✓
Metaproterenol (S)	✓		
Pirbuterol (S)	✓		
Salmeterol (L)		✓	
Terbutaline (S)			
Corticosteroids			
Fluticasone	✓	✓	
Budesonide		✓	✓
Flunisolide	✓		
Triamcinolone acetonide	✓		
Mometasone furoate		✓	
Ciclesonide	✓		
Anticholinergics			
Ipratropium bromide	✓		
Tiotropium bromide		✓	

MDI = metered-dose inhaler; DPI = dry powder inhaler; L = long-acting; S = short-acting.

of efficacy. This is the conclusion of a large systematic meta-analysis taking in Medline, Embase, and the Cochrane Library.¹⁷ The study included a total of 254 randomized controlled trials that compared different types of devices against each other, primarily concerning beta₂-agonists. Some types of device were under-represented in the meta-analysis, notably breath-actuated pMDIs. Nevertheless, the authors concluded that “none of the pooled meta-analyses showed a significant difference between devices in any efficacy outcome in any patient group. Each of the devices studied can work equally well in patients who can use them appropriately.”

The emphasis, however, is on correct use of each device, and it is important that proper training be given regardless of the device chosen. Thus, when a clinician needs to select a device for a patient’s regular use, the main factors to consider include personal preference, practicality, and cost. The primary consideration is which devices are available with the medication required; not all drugs are available with all types of inhaler (see Table 2). If multiple medications are required, selecting a device that is common to them all will minimize errors; patients are more likely to get confused when they have to use different types of inhalers.¹⁸ Age and the mental and physical capabilities of the patient are clearly limiting factors in device

selection as well. National guidelines and recommendations for device selection are generally based on a patient's age.^{4,3,19} For young children under four years of age, most guidelines recommend use of a pMDI with a spacer and a face-mask or a nebulizer with a face-mask. Between four and five or six years of age, the face-mask can be replaced by a mouthpiece, while after five or six years of age the child can generally cope with a DPI or one of the types of pMDI.^{3,21}

In summary, the choice of device is as important as the medication in treating asthma. While targeting the lungs directly with inhaled medication is not a new concept, device technology has come a long way in the last 60–70 years. While the perfect inhaler has yet to be made, newer devices are coming closer. Until it arrives, there is still a huge array of choice in terms of inhalers, all of which, if used correctly, are equally effective. Thus, patient choice, cost, and practicality issues will generally determine the right one to use. ■

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