Delivering inhaled asthma therapy

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SYNOPSIS

There is a wide range of devices for delivering inhaled therapy. Metered dose inhalers are commonly used, but the introduction of formulations without chlorofluorocarbons will require practitioners to reassess their patients' therapy. Nebulisers, pressurised devices and dry powder preparations are all effective. The most important issue is to ensure patients use their devices correctly and adhere to their treatment plan. Recent meta-analyses show that nebulisers, although convenient in acute attacks, have no sustained advantage over pressurised devices with or without spacers.

Index words: inhalers, nebulisers, spacers, devices.

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Introduction

Inhaled medication is the commonest form of therapy for acute and chronic asthma and for other conditions associated with airflow limitation (obstructive bronchitis, emphysema, cystic fibrosis). There are over 50 separate listings of inhaled medications in the respiratory drugs section of the current Schedule of Pharmaceutical Benefits (Table 1). The choice of inhalational device is as important as the choice of drug therapy.

Theoretical considerations

There is a strong logic in giving drugs which act on the bronchial tree by the inhaled route. The delivery is directly to the site of pathology and the large surface area available for absorption should lead to a rapid response. There is no need to obtain significant concentrations in the blood so the incidence or extent of unwanted adverse effects is reduced.

The fate of an inhaled medication within the respiratory tract is determined by complex physical factors. However, the most important relate to particle size and breathing patterns. Particles with a median mass diameter greater than 10 microns tend to be deposited in the upper respiratory tract and those smaller than 0.5 microns behave as gases and are exhaled. Deposition within the lower respiratory tract increasingly occurs as the particle size decreases from 4 to 2 microns.

Nebulisers

A pump/nebuliser system has several attractions:

- administration does not require close supervision
- co-ordinated breathing manoeuvres are unnecessary
- combinations of drugs may be given simultaneously
- it is suitable at extremes of age
- the dose delivered, among other factors, is a function of time.

Currently available models are surprisingly efficient and have an average output of 1–2 mL over 10 minutes with about 30–50% of the output being as a respirable aerosol.

Weighed against these attractions are the considerable cost compared with simpler devices, the wastage of nebulised drug during exhalation and the fact that delivery of larger doses does not translate into better therapeutic responses. This is because there is a dose-response relationship which reaches a plateau so that delivering a larger dose via a nebuliser will produce no further bronchodilatation. A recent meta-analysis (16 trials, 375 adults, 686 children) concluded that metered dose inhalers with holding chambers (spacers) produced outcomes at least equivalent to nebuliser delivery.[1]

While the actual nebuliser unit is not expensive (about $18 retail), the driving source, which is usually a small compressor unit, costs between $180 and $480. It requires minimal maintenance and a good quality device should last 5–10 years. The economics of the nebulised solutions are relevant. Single dose units, although convenient, are nearly three times more expensive than the multidose preparations.

Nebulisation is still necessary for preparations which are not available in other devices (for example, pentamidine prophylaxis against *Pneumocystis carinii*, mucolytics and rhDNase in cystic fibrosis). Most international guidelines dealing with the treatment of acute asthma in adults recommend a place for a nebulised short-acting beta agonist, using oxygen as the driving gas.[2] However, the current tendency is to use a pump/nebuliser system only when there are valid reasons for doing so rather than as a first-line approach to inhalational therapy.

Ultrasonic nebulisers have little if any place in asthma therapy. They are expensive and deliver an efficient aerosol which, because of the very fine particle size, can lead to difficulties with dose retention.

Metered dose inhalers

Metered dose inhalers have been enthusiastically accepted and perform well when compared with all other forms of administration.[3] They are very convenient and provide accurate doses which can be readily adjusted by changing the number of actuations. Using an inhaler requires some level of understanding and a major problem with their use is inappropriate technique. It is always good practice to show the patient how to use an inhaler and subsequently check their technique. The important points are:

- timing of activation (at the commencement of inspiration from functional residual capacity)

- inspiratory flow rate (full lung inflation in about two seconds)
- breath-holding time at the end of inspiration (at least three seconds and preferably up to 10 seconds).[4]

Pressurised inhalers with hydrofluoroalkanes as the propellant (Table 1) have been developed to comply with the Montreal Protocol (to reduce and phase out the use of chlorofluorocarbons (CFCs)). By 2005, there will be no inhalers containing CFCs. Several products were withdrawn during 2002.

It is important to realise that the CFC-free inhalers produce a finer particle size and hence lead to a more effective lung deposition. This means that the actual dose required is less for the same brochodilator effect and the product information should be read carefully. In practice the 'numbers of inhalations' between CFC and non-CFC preparations are roughly equivalent.

Breath-activated pressurised inhalers

Clever technology has seen the development of devices in which the pressurised inhaler is triggered by the reduction in pressure associated with the onset of inspiration. This avoids difficulties some patients have in co-ordinating manual triggering with early inspiration. These devices are more expensive and thus have prescribing restrictions in the Pharmaceutical Benefits Scheme (PBS).

Dry powder inhalers

Devices delivering drugs in a dry powder are an alternative to propellant driven inhalers. Patients initially tend to distrust the performance of these devices since they do not produce a visible aerosol and there is no sensation of having inhaled the minute amount of powder delivered. These devices appear to be just as convenient and efficient as the pressurised inhalers and they are reassuring for patients concerned about the environment.

Combination therapy

In the past, combination therapy in a single commercial product was viewed with some disdain, as fixed dose ratios do not allow individual tailoring of doses. To some extent this criticism has been outweighed by the likelihood of better adherence to a regimen if the number of inhalers is reduced. Preparations including a long-acting beta agonist and inhaled corticosteroid have been readily accepted although the various dose combinations require some juggling and their prescription under the PBS remains restricted. Combination therapy is not satisfactory in the management of an acute exacerbation.

Spacers

There are several commercially available spacers and some are specifically constructed to attach only to a specific

Table 1

Inhaled preparations currently listed on the Pharmaceutical Benefits Scheme for asthma

Device	*Advantages*	*Disadvantages*	*Products available*
Nebulising solution	No co-ordination required Suitable at extremes of age	Initial cost Equipment maintenance Wasteful drug use	Salbutamol sulfate Terbutaline sulfate Ipratropium bromide Budesonide Sodium cromoglycate
Dry powder preparation	Convenient	No sensation of inhaling active drug	Salbutamol sulfate Salmeterol xinafoate Eformoterol fumarate Terbutaline sulfate Budesonide Fluticasone propionate Sodium cromoglycate Eformoterol/budesonide Salmeterol/fluticasone
Pressurised inhaler	Convenient	Being phased out Co-ordination required	Salmeterol xinafoate Ipratropium bromide Sodium cromoglycate Salbutamol/ipratropium*
Pressurised inhaler CFC-free	More uniform lung deposition	Co-ordination required Dose adjustment considerations	Salbutamol sulfate Beclomethasone dipropionate Fluticasone propionate Sodium cromoglycate Salmeterol/fluticasone Nedocromil sodium
Breath-triggered pressurised inhaler	No co-ordination required	More expensive	Ipratropium bromide
Breath-triggered pressurised inhaler CFC-free	No co-ordination required More uniform lung deposition	More expensive Dose adjustment considerations	Beclomethasone dipropionate Salbutamol sulfate

* Repatriation Pharmaceutical Benefits Scheme only

inhaler. They are somewhat bulky and therefore tend to be used at home.

Spacers fulfil two functions. First, they allow the larger particles within the aerosol generated by an inhaler to rain out within the chamber. The inhaled portion has a higher proportion of finer particles which should improve deposition within the lungs and reduce oral deposition. This reduces the incidence of oral thrush, however mouth gargling with clean water after inhalation is still important. Second, the larger chambers, with a one-way valve at the mouthpiece, can retain an aerosol in suspension while the patient inhales that suspension without the need for special co-ordination. Spacers can be used for single breath actuation, but an alternative is to deliver the total dose (e.g. two activations) into the spacer and inspire from the spacer over several breaths. This is a great advantage in very young patients, the elderly and the unco-ordinated. As the medication becomes attached to the walls of the chamber, spacers need cleaning about every two weeks using warm soapy water. They should be left to dry out naturally to avoid accumulation of static charge by towelling.

Conclusions

Factors to consider in choosing a device to deliver asthma therapy include the patient's age, level of understanding and co-operation, and extent of co-ordination. A trial period with a device will often reveal problems with compliance or individual preferences. The wide variety of devices and preparations does not alter the eternal truth that the most important aspect of inhalational therapy for chronic respiratory diseases is to establish and maintain correct usage and faithful adherence to an overall plan of management. The actual drug chosen within a particular class of medication is of secondary importance.

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Conflict of interest: none declared

Patient Support Organisation: Asthma Australia. See details on page 21.

Self-test questions

The following statements are either true or false (answers on page 23)

1. Spacers should not be dried with a towel.
2. Beta agonist bronchodilators are more effective when delivered by nebuliser than when they are given by a metered dose inhaler through a spacer.

Online reporting of adverse drug reactions

Australian Prescriber readers are now able to report adverse drug reactions directly to the Adverse Drug Reactions Advisory Committee (ADRAC). A new computer system will also allow readers to request information from the database of adverse reactions.

Health professionals who are likely to use the new service regularly can become 'registered reporters'. Those who just wish to report reactions occasionally can do so as 'unregistered reporters'.

To access the service, people can connect to the web site of the Therapeutic Goods Administration (www.health.gov.au/tga). They can then click on the 'Online Services' button and follow the links.

The Adverse Drug Reactions Advisory Committee is planning further electronic developments. From later this year it should be possible for general practitioners to submit reports of adverse reactions if they use prescribing software on their practice computers.

For health professionals who do not use computers, reports can still be mailed using the 'blue card'. Copies of the blue card are distributed with *Australian Prescriber* four times a year.