Leading articles

How to choose delivery devices for asthma

The inhalation route has many advantages in the treatment of diseases of the respiratory tract. Medication may be delivered directly to its site of action, giving a faster onset and allowing smaller doses of drug to be administered. Systemic absorption of the drug is diminished, reducing systemic side effects. The drug treatment regimen for the vast majority of patients with asthma is straightforward and is documented in recent guidelines.[1] The choice of which drug delivery device to use is less clear. Rather than being spoilt for choice, we are more frequently confused by the ever increasing number of devices available. What guidance may be given to the paediatrician selecting an inhalation drug delivery device for a patient? The choice depends on the device, the patient, and the drug. Our current practice is outlined in table 1.

Spacer devices, used with facemasks for children unable to breathe reliably through a mouthpiece, are the first choice of device for children younger than 5 years. Nebulised delivery of bronchodilator and prophylactic medications is inefficient and expensive, and nebulisers should be reserved for those unable or unwilling to use metered dose inhalers and spacers. The use of metered dose inhalers alone, breath actuated devices, and dry powder inhalers should be discouraged in this age group. It is important to read studies pertaining to this age group with care, as conclusions of a device's suitability may be generated across a wide age range, despite inclusion of a small number of subjects younger than 5 years chosen for their ability to undertake advanced respiratory manoeuvres.

For children older than 5 years, bronchodilators may be given via a breath actuated metered dose inhaler or a dry powder inhaler. We recommend a spacer device for the administration of inhaled steroids at any age. These are normally given twice a day, for instance on waking and retiring, so arguments that the spacer is not portable are not relevant. However, for low dose steroids, if the child is unwilling to use a spacer, breath actuated or dry powder devices may be chosen in preference to the metered dose inhaler alone. There is no evidence that changing to these devices improves compliance.

Drug delivery device

There are three main types of inhalation drug delivery device, grouped by the drug dispersion method that they use: pressurised metered dose inhalers, containing a mixture of propellant and drug under pressure; dry powder inhalers, utilising the patient's inspiratory effort to disperse medication; and nebulisers, using compressed gas or the vibration of a piezo electric crystal to aerosolise liquids. Adjuncts—such as spacers or holding chambers—may also be used to improve inhalation treatment.

PRESSURISED METERED DOSE INHALERS

Pressurised metered dose inhalers are easy to actuate, but difficult to use properly. Drug is emitted at high speed and most impacts in the oropharynx. Many adults and most children use their metered dose inhalers incorrectly,[2] and the necessity to coordinate inhalation with metered dose inhaler actuation means that they are not suitable for use on their own for most children.

Metered dose inhalers with extended mouthpieces, such as the Spacehaler (Evans Medical, Leatherhead, UK), are designed to reduce the speed of the emitted aerosol, reducing oropharyngeal deposition. There are no published studies of this device used by children.

Breath actuated metered dose inhalers incorporate a trigger that is activated during inhalation. In theory, this reduces the need for the patient or carer to coordinate metered dose inhaler actuation with inhalation.[3] However, patients may stop breathing when the metered dose inhaler is actuated (the "cold freon effect") or have suboptimal inspiration.[4] Evaluation of their efficacy in children under the age of 6 years is limited,[5] and their use should be restricted to older children and adults. Oropharyngeal deposition of steroids using these devices is still very high, and some devices incorporate a short open tube spacer. This addition may be expected to reduce extrathoracic drug deposition, although there are no published evaluations of its use.

Spacer devices were developed to overcome some of the problems of metered dose inhalers. There are two main types.

Table 1 Age specific recommendations for drug delivery devices

Age (years)	*First choice*	*Second choice*	*Comments*
0–2	MDI + spacer and facemask	Nebuliser	Ensure optimum spacer use Avoid "open vent" nebulisers
3–6	MDI + spacer	Nebuliser	Very few children at this age can use dry powder inhalers adequately
6–12 (bronchodilators)	MDI + spacer, breath actuated or dry powder inhaler	–	If using breath actuated or dry powder inhaler, also prescribe MDI + spacer for acute exacerbations
6–12 (steroids)	MDI + spacer	Dry powder inhaler	May need to adjust dose if switching between inhalers Advise mouth rinsing or gargling
12+ (bronchodilators)	Dry powder inhaler or breath actuated MDI	–	
12+ (steroids)	MDI + spacer	Dry powder inhaler or breath actuated MDI	May need to adjust dose if switching between inhalers Advise mouth rinsing or gargling
Acute asthma (all ages)	MDI + spacer	Nebuliser	Ensure optimum spacer use and appropriate dosing Nebulise for a set period of time Written instructions for what to do in acute asthma

MDI, pressurised metered dose inhaler.

Valved holding chambers (for example, Volumatic (GlaxoWellcome, Uxbridge, UK), Nebuhaler (AstraZeneca, Kings Langley, UK), Babyhaler (GlaxoWellcome), Aerochamber (Trudell Medical, Ontario, Canada) are what most practitioners refer to as spacer devices. They allow the patient to breathe tidally from a reservoir of drug. Facemasks allow spacers to be used by infants and children too young to use a mouthpiece. However, delivery of drug by a mouthpiece is more efficient, and patients should use this in preference to a facemask as early as possible.

Extension devices may be used with pressurised metered dose inhalers. They provide a "space" between the inhaler and the patient, allowing the aerosol to slow and propellants to evaporate, reducing the size of drug particles from metered dose inhalers, and trapping large particles in the spacer. Examples include the Integra for becloforte, the Optihaler, and ACE spacer. Coordination is still required for optimal drug delivery. Because of this, these devices are not suitable for young children and may be inappropriate for the large number of patients, of any age, who have difficulty in coordinating actuation of a metered dose inhaler and inhalation.

The size of the spacer may also affect the amount of drug available for inhalation, and this will vary with the drug prescribed.[6–8] The clinician should be aware that data about a spacer derived from studies with one drug might not apply to others. Similarly changing from one spacer to another may be unimportant with some drugs, but be critical for others, leading to overtreatment or treatment failure. Output from spacer devices may vary greatly depending on static charge. Drug output from a spacer lined with an antistatic agent may increase by a factor of 3 or more. Static charge of polycarbonate spacers will vary greatly depending on the washing procedure used and the use of the spacer. Although non-electrostatic spacers should overcome this variability they are not currently available in the UK.

DRY POWDER INHALERS

Dry powder devices do not have the associated problem of coordination difficulties experienced when a metered dose inhaler is used. However, oropharyngeal deposition of inhaled drug is high, and spacer devices are still advocated for patients requiring higher doses of inhaled steroids. In the UK, the Accuhaler (Discus (GlaxoWellcome))[9] and the Turbohaler (AstraZeneca)[10] are the most popular. Comparative studies of these two multidose devices are confusing. The Accuhaler is twice[11] or equally[10] efficient at delivering medication as the Turbohaler. In vitro studies suggest that the Accuhaler is more consistent in the dose delivered at different flow rates, although it has a reduced fine particle mass and emits more large particles than the Turbohaler.[12] Again the number of dry powder inhalers are continuing to increase. The Clickhaler device (Medeva, Leatherhead, UK) is designed to look similar to a metered dose inhaler, even mimicking the press down action of a metered dose inhaler to load a unit dose for inhalation.

NEBULISERS

Nebulisers are mentioned only briefly because of their decreasing role in asthma management. Many new designs have been introduced without formal information on the output of drugs such as steroids being available. This is of concern as recent laboratory studies have shown that the amount of budesonide a child is likely to inhale from different devices may vary by up to 400%.[13] Most of the prescribed medication for nebulisers never reaches the lungs. Of the dose placed in the nebuliser chamber, perhaps two thirds remains there at the end of nebulisation. Two thirds of the dose released from the nebuliser may be released during expiration and passes into the surrounding air. With many nebulisers, less than 10% of the prescribed dose reaches the lung. The nebuliser does not rely on patient cooperation or coordination to work, although deposition is improved by the use of a mouthpiece rather than a facemask, by holding the facemask close to the patient,[14] and by the patient breathing quietly, rather than crying or rapid breathing.[15]

The Halo-lite (Medicaid, Pagham UK) is the only nebuliser currently able to release a predetermined dose with accuracy.[16] It monitors the breathing pattern of the patient, generates pulses of aerosol during early inspiration only, and allows titration of the inhaled drug dose. As the patient's breathing pattern is known to affect the delivery of drug from nebulisers, this type of device may prove more efficient and reliable than conventional nebulisers, although no published studies have examined this device when used by children. The inclusion of electronic devices used to monitor compliance, currently used in research trials, would be of great help in monitoring asthma patients who are responding poorly to treatment.

Dose variability with age

The patients' breathing pattern will affect the dose of drug delivered from a nebuliser or spacer device.[15] The amount of drug delivered from a polycarbonate spacer increases with tidal volume,[17] and more drug may be delivered from small rather than large volume spacers when these are used by infants and young children.[18]

From nebulisers, the inhaled dose increases with age up to the point where inspiratory flow exceeds nebuliser output,[19] and the dose inhaled per kilogram is constant up to 6 months of age, declining after this. Only infants will inspire with a lower flow than that of the nebuliser output, and only then will the dose received be affected by the child's size. The importance of this observation has been highlighted in relation to bronchoprovocation studies in infants and young children.[20] Data from Salmon *et al* suggests that up to 1.5% of the dose of nebulised sodium cromoglycate will be deposited in the lungs of children from 6–36 months of age.[21] Assuming approximately 10% of a nebulised dose is deposited in the lungs of an adult, the dose per kilogram body weight can be calculated. For example, a 70 kg adult will receive 0.14%/kg (10% ÷ 70), whereas, using Salmon's data, young children will receive up to 0.15%/kg (1.5% in a 10 kg infant). This suggests that although there may be poor drug deposition in infant lungs, this is compensated for by their small size, so that the final dose reaching the lungs per kilogram body weight may be very similar to that of an adult.

There have been few clinical studies of lung deposition of nebulised aerosols in children. Alderson *et al* found that lung deposition increased with age,[22] whereas others[23 24] have found no relation between age and total lung deposition of nebulised aerosols.

Compliance

The most effective inhaler for any given patient is the one that the patient will use on a regular basis and in an effective manner. Patient compliance with inhaled medication is poor. In studies using electronic timer devices attached to metered dose inhalers, where subjects knew that compliance was being monitored, on only half of the study days was the prescribed medication taken, whether this was self administered by adults or children[25 26] or where administration was supervised by a parent.[27] Poorly compliant

patients are at increased risk of exacerbations.[28] Although there is no evidence that compliance is improved by changing to a different inhaler device, small, unobtrusive devices are often marketed on the basis that they are more acceptable to the patient, and will therefore be used more. There is increasing interest in drug delivery devices that can both monitor and prompt patient use.

Conclusions

Age and drug specific recommendations can be made (table 1), and are a useful starting point. At present clinical management should be based on prescribing a device that the patient will use, and encouraging adherence to prescribed treatment. Clinicians should be aware of the limitations of each type of device, and the optimum methods of use for each. They should then pick one or two of each type of device for use in their practice and become completely familiar with these, using table 1 as a guide. When considering new devices, clinicians should ask how the devices were tested, and whether the tests are appropriate to estimate lung deposition. Whichever device is used the dose of drugs, such as corticosteroids, should be titrated to the lowest dose required to control symptoms.

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Pectus excavatum: studiously ignored in the United Kingdom?

Pectus excavatum describes a malformation of the anterior chest wall characterised by a hollowing over the sternum and an associated prominence of the costochondral junction. The resulting depression in the chest wall, the opposite situation to pigeon chest (pectus carinatum), is variable in severity, ranging from a mere indentation to an extreme form where the sternum lies within a few centimetres of the vertebral column. The reported incidence is eight per 1000 population, more commonly in boys. It might be anticipated that such a deformity would have significant implications for cardiorespiratory function and pose a cosmetic challenge.

Patients with pectus excavatum have a mild restrictive ventilatory defect,[1] but functional impairment is difficult to demonstrate, appearing at only the extreme limit of exercise tolerance.[2] Despite an increase in the intrathoracic volume postoperatively, there is no substantial associated improvement in pulmonary function.[3]

The North American and [continental] European literature abound with references to various aspects of this condition: the possible benefits of surgical treatment, the complications of such operations, and the psychological burden associated with the condition. Such literature reveals that pectus surgery is commonplace in these societies, with series of many hundreds of cases being reported.

The British literature is strangely silent, contributing fewer than 5% of articles cited in MEDLINE in the past 10 years. Equally, the referral rate to paediatricians and paediatric/thoracic surgeons appears to be very low, although we are currently conducting a survey of paediatricians with a respiratory interest in Wessex and the South West to quantify this.

It is undoubtedly true that, unlike their North American colleagues, British paediatric surgeons see very few children with chest wall deformities and there is an overall impression that patients are simply advised to put up with their deformity.

While obviously disfiguring, even the most trenchant pectus surgeons recognise that correction of the deformity will not usually give significant physiological benefit. The fact that in the face of this North American surgeons are prepared to perform extensive surgery with significant complications implies that they recognise the psychosocial burden[4] of such an obvious abnormality. While formerly, the cynic might have pointed to a fee for case arrangement as a motivating factor, modern risk management would have curtailed such activities—but on the contrary, pectus surgery is flourishing.

The surgery of gynaecomastia in adolescence bears comparison. This condition is known to resolve spontaneously in the vast majority of cases, but the psychosocial