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Metered dose inhalers and spacer devices

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Abstract. – **Easy to carry, highly effective and extremely safe, allowing accurate, consistent dose delivery, metered dose inhalers are the inhalation devices doctors and patients choose most readily the world over.**

Clinical response, however, may be affected by the inhalation technique used and the precise formulation in the canisters.

The purpose of this review is to consider metered dose inhalers, add on devices and training issues related to the proper coordination of drug delivery with inhalation, and to report on new technology and recent studies into non ozone depleting propellants, in compliance with the Montreal protocol.

Key Words:

Metered dose inhaler, Aerosol, Particle size, MMAD, Inhalation technique, Propellants, Spacer device, Holding chamber.

Introduction

Metered Dose Inhalers (MDIs), developed in 1956[1], are the most widely used devices for aerosol therapy. Over 70 million patients in the world use a metered dose inhaler[2] either alone or in association with a spacer.

An MDI consists of a canister containing a drug in suspension or in solution with surfactants, lubricants and a propellant, at a pressure of approximately 3 atmospheres, depending on the type of propellant used. The canister is lodged upside down in a plastic support. By pressing the bottom of the canister, a premetered drug dose is released. A small amount of surface-active agents (e.g. sorbitan trioleate) is usually added to the formulation, to help reduce particle aggregation and to lubricate the delivery valve.

MDIs are designed to deliver a number of drug doses in a sequence (usually, up to 200). They are quick to use, portable and relatively inexpensive. In order to obtain correct drug delivery and deposition, however, a special technique is required (i.e. very good co-ordination between device actuation and inhalation, which must take place simultaneously). For this reason, children and elderly patients find the devices difficult to use (the latter, in particular, in cases of osteoarticular disorders affecting the hands). The main problems connected with the use of MDIs[3-5] are shown in Table I.

In addition, coordination between aerosol actuation and breathing-in (which must occur simultaneously) is required, and some problems arise from the use of propellants which, by boosting particle speed, facilitate deposition in the oro-laryngeal tract.

Failure to clean the mouthpiece and drug delivery outlet may also affect consistency of the dose and aerosol particle size.

In addition, it is common practice to advise patients to check the filling level by placing the canister in a bowl of water.

This practice should be discouraged since water can enter the canister through the valve actuator.

Assuming the canister is working properly, a better method is to count the doses as they are inhaled. For example, a canister with 200-dose capability, used twice a day with 2 doses each time, empties in 50 days.

In MDIs, the delivered aerosol particle size distribution depends on the time required for the propellant to evaporate. Unlike in dry powder inhalers, their hygroscopic properties are of little importance.

At the metering valve outlet, the MMAD (Mass Median Aerodynamic Diameter) is 30-40 µm, while at a distance of approximately 10 cm from the valve (Table II) it decreases to as low as 1.7 µm[1] (Figure 1).

The final result is a mixture of particles in solutions and suspensions with non-volatile additives, the mass concentration of which

Table I. Main problems connected with the use of MDIs.

- Canister not shaken energetically before delivery
- Mouthpiece cap not removed
- Patient breathes in before delivery
- Patient breathes in after delivery
- Patient breathes out during delivery
- Patient breathes in through the nose
- Patient delivers multiple doses during the same breath
- Drug delivery and inhalation are not simultaneous
- Inhalation is interrupted due to "Freon effect" (early breath cut off caused by a cold sensation provoked by CFCs in the pharynx)
- Patient breathes out before inhalation is complete

ranges from 0.1% to 1% according to the individual case[6].

Particle velocity near the delivery outlet is approximately 50 m/s, decreasing rapidly to approximately 10 m/s[7-11] at a distance of 10 cm from the valve.

On release the particles take on the characteristics of heterodisperse aerosols with various shapes, ranging from spherical to elliptical. Particle diameter depends on propellant evaporation time and on particle distance from the delivery outlet.

For effective particle deposition in the lower airways, the aerodynamic diameter of particles should be < 5 μm[12]. However, particularly for patients with obstructive lung disease, all particles should ideally be within the 2-3 μm range[13-15].

The distance between the delivery valve outlet and the oropharynx surface (where the propellant has not completely evaporated) is approximately 10 cm; it is therefore recommended that metered inhalers be used by delivering the drug at a distance of approximately 8-10 cm from the mouth, making sure that canister actuation is co-ordinated with inhalation (slow and deep rather than quick and superficial, to prevent particle inertial impact on the oropharynx and upper airways and to help particle gravitational sedimentation in the respiratory tree).

This procedure leads to better particle micronization, reduces the number of particles likely to impact on the upper airways (due to their greater size and velocity), and allows smaller particles (slower, and following the inspiratory flow) to settle in the deep lung.

Hence, the size of the particles delivered by MDIs is influenced by a variety of factors, including:

1. Pressure inside the canister;
2. Physical and chemical properties of the propellant and of the other additives;

Table II. Mass Median Aerodynamic Diameter of drugs delivered via CFCs-MDI. Measured with API Aerosizer Mach[2] (1).

Drug	Brand	Manufacturer	Dose per puff	MMAD (μm) [SD]
Fluticasone propionate	Flixotide Mite	Glaxo Wellcome	50 mcg	1.74 [0.15]
Fluticasone propionate	Flixotide Glaxo	Wellcome	125 mcg	1.98 [0.32]
Fluticasone propionate	FlixotideForte	Glaxo Wellcome	250 mcg	3.85 [0.59]
Bechlomethasone dipropionate	Clenil Forte	Chiesi	250 mcg	4.13 [0.44]
Flunisolide	Nisolid	Master Pharma	250 mcg	3.46 [0.58]
Salbutamol	Ventolin	Glaxo Wellcome	100 mcg	2.28 [0.24]
Salmeterol	Salmetedur	Glaxo Wellcome	25 mcg	2.85 [0.19]
Formoterol	Foradil	Novartis	12 mcg	2.69 [0.26]
Procaterol	Propulm	Istoria	10 mcg	3.27 [0.29]
Procaterol	Propulm	Istoria	25 mcg	3.87 [0.33]
Ipratropium bromide	Atem	Chies	20 mcg	2.62 [0.15]
Oxitropium bromide	Oxivent	Bohringer Ingel	100 mcg	3.79 [0.3]
Sodium cromoglycate	Lomudal	Rhone Poulenc R.	5 mg	8.1 [1.32]
Nedocromil sodium	Tilade	Rhone Poulenc R.	2 mg	4.64 [1.14]

Data showing that drug concentration and other factors such as physical and chemical properties of drugs, manufacture and design of the MDI device may affect the MMAD.
SD: Standard Deviation.

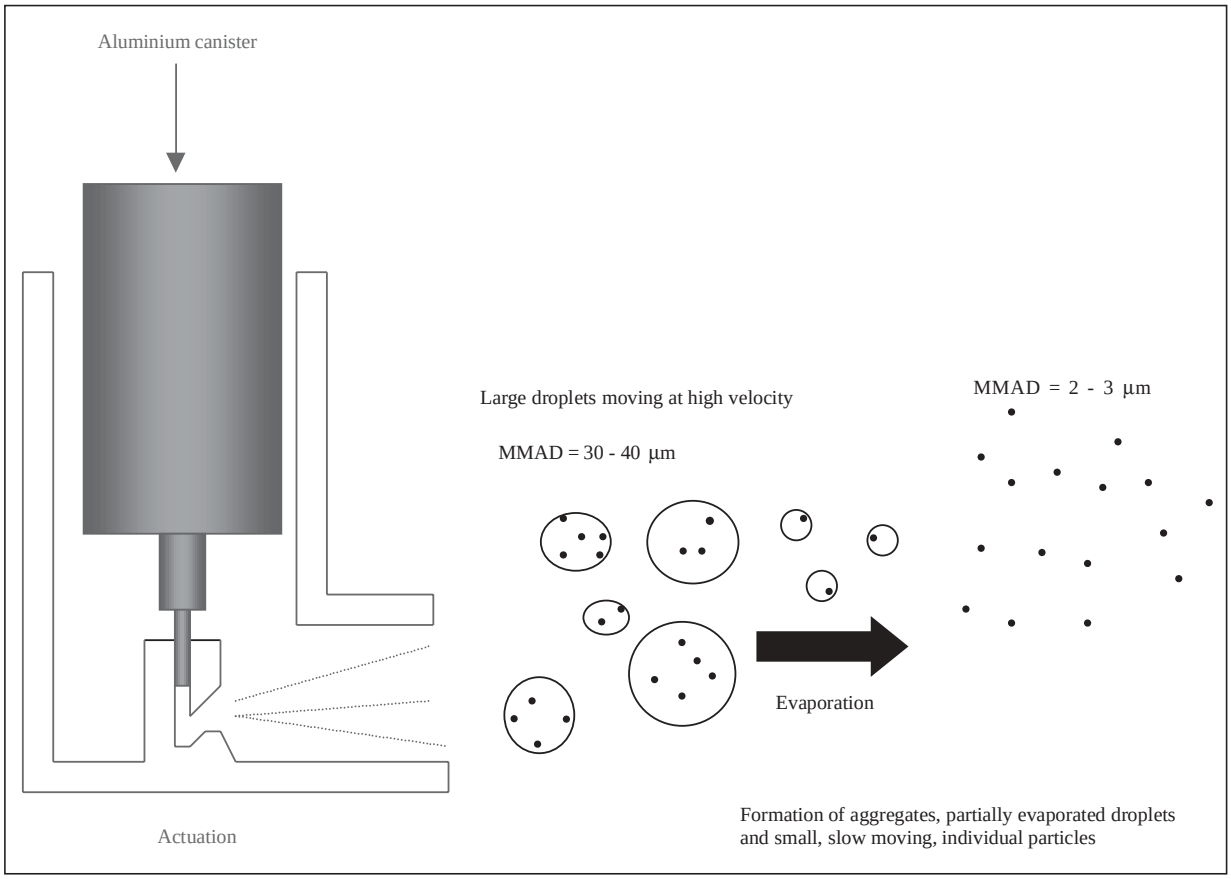

Figure 1. Diagram of a typical pressurized metered dose inhaler showing mechanism of particle formation. *MMAD = Mass Median Aerodynamic Dyameter.*

3. Drug used and its concentration and delivered volume;
4. Metering valve and delivery outlet design;
5. Mouthpiece and delivery outlet cleanness.

The canister contains the drug in powder form in a micronized suspension in the liquid propellant or in the form of a drug solution added to the propellant and other additives. As soon as the metering valve is actuated, a mixture of gas and liquid is formed which then expands volumetrically beyond the outlet.

Metering valve and delivery outlet design are critical because nebulization decreases dramatically as the particle diameter increases. A large delivery outlet diameter generally produces large-sized particles, while a small diameter can cause outlet clogging. In addition, particles which are too small tend to re-aggregate, resulting in an increase in their diameters[11,16-31].

Failure to shake the canister well before use is a common cause of variability of drug doses. The drug powder suspended in the propellant may be less dense than the propellant; in this case, if the canister is left to rest on its support without shaking, the drug gradually separates from the suspension, forming a supernatant over the mixture of propellant and other additives. The immediate consequence is a decreased drug concentration in the metering valve area.

Conversely, in cases where the drug has a higher density than the propellant, it tends to settle in the metering valve area, with a resulting increase in concentration levels in that area[32]. Other faults which can be observed in MDIs are listed in Table III.

Table IV lists technical aspects related to MDI use tending to influence drug deposition in the lower airways.

Table III. Construction faults observed in MDIs.

1. Delivered dose higher than the design dose
2. Delivered dose lower than the design dose
3. Device works only occasionally
4. Device releases a lower number of doses than expected
5. Delivery outlet clogs prematurely

The use of these devices requires a proper inhalation technique. Like all other types of inhalation device, (dry powder inhalers, nebulizers, spacers), MDIs require careful explanation and training before use, provided mainly by medical staff.

Experience shows that the open mouth technique (Table V), which requires repeated correction during follow-up visits, leads to more thorough drug deposition[33] in the lower airways (with improved therapeutic response) than the sealed lip technique (Table VI).

New prospects: advanced propellants and techniques

Propellants most commonly used are chlorofluorocarbons (CFCs): trichlorofluoromethane (P-11), dichlorodifluoromethane (P12) and dichlorotetrafluoroethane (P14), usually mixed.

Additives such as surfactants (lecithin and oleic acid) and solvents (ethanol), present in the canister in a mixture with the drug and the propellant, are known to have caused bronchospasm response in predisposed subjects[41].

In addition, particle concentration in the aerosol depends on surfactant concentration (the smaller the amount of surfactant, the lower the aerosol particle concentration) and is independent of the propellant pressure inside the MDI, which has a strong effect on particle size distribution: the particle diameter tends to decrease as the delivery pressure increases, as is the case with nebulizers when the compressor delivery pressure is increased[42], and/or surfactants such as ethanol or propylene glycol are added to the aerosol solution.

CFCs have been used as propellants not only in metered dose inhalers, but also in refrigerating systems and air conditioning installations. CFCs are considered essential for MDI manufacturing, and are still available today exclusively for use in these devices, although it is expected that they will be replaced before the year 2005 by other propellants, such as hydrochlorofluorocarbons (HCFCs), hydrofluorocarbons (HFCs) and hydrofluoroalkanes (HFAs). Of these, HFA-134a and HFA227 have proved to be well tolerated by patients[8].

The propellants most commonly found in MDIs today are in the chlorofluorocarbon (CFCs) class. Although it is possible to use CFC12 alone, they are usually found as mixtures[43] of two or three different CFCs: CFC11, CFC12, CFC114 at a vapour pressure of 13.4 psia at 21°C and a boiling point of 23°C (CFC11) or with a vapour pressure of 85 psia at 21°C and a boiling point of 29.8°C, in the case of CFC12, whose characteristics make it a far stabler product. CFC114, frequently used in association with CFC12, is known as a mild solvent for medical products. Very stable, it has a vapour pressure of 28 psia at 21°C and a boiling point of 3.6°C.

The aim of CFC mixtures is to produce the physical and chemical properties necessary for

Table IV. Technical aspects relating to MDI use tending to influence drug deposition in the lower airways.

Inhalation technique	*Drug dose reaching the lungs*
Poor delivery/inhalation timing	As low as 0% of the expected dose
Quick inhalation and 10 seconds' end-inspiratory pause in a patient with very good timing	Approximately 7% (34)
Slow inhalation and 4 sec. end-inspiratory pause	Approximately 6.5% (34)
Slow inhalation and 10 sec. end-inspiratory pause	Approximately 14% to 50% (34-36)
Delivered volume: 25 µl	Approximately 17% (37)
Delivered volume: 50 µl	Approximately 12% (38)
Delivered volume: 100 µl	Approximately 9% (39)
Failure to shake the canister	Approximately 50% of the expected dose (40)

Table V. Open mouth technique.

1. Remove the mouthpiece cover
2. Shake the MDI energetically
3. If it is a new device, carry out three blank tests making sure you shake the canister well between one actuation and the next
4. Turn the device upside down (mouthpiece facing down)
5. Position the device at a distance of 8/10 cm from your mouth (keeping your mouth open)
6. Breathe out slowly and thoroughly
7. Press the canister bottom and at the same time, breathe in slowly and deeply
8. Hold your breath for approximately 10 seconds
9. Shake the device again and one minute later, repeat the procedure from 4 to 8 if prescribed by your physician
10. Regularly check that the delivery outlet and the mouthpiece are perfectly clean inside and outside

ideal drug release and drug dispersal in the form of particle sizes suitable for inhalation.

New propellants, such as hydrofluoroalkanes (HFA): P-134 (trifluoromonofluoroethane: vapour pressure of 85 psia) and P-227 (heptafluoropropane: vapour pressure of 58 psia) have been developed, with different features from CFCs, in that they do not contain chlorine and, unlike CFCs, have limited effects on ozone depletion. Metered dose inhalers containing P-134a, in particular, have a much higher vapour pressure than those containing CFCs.

New CFC-free MDIs, containing albuterol sulphate and bechlomethasone dipropionate, have been developed and have proved in some cases as effective as devices containing CFCs, both in terms of bioequivalence and in terms of efficacy and safety[44-46]. In these devices, the mouthpiece was redesigned and the valve components and particularly the gaskets[47] were modified to suit the new propellant, although delivered dose consistency requires further study.

P-134a and P-227 are likely to be delivered at a greater speed than CFCs, due to the much higher pressure required to reach the liquid state compared to CFCs. For this reason, metering valves using P-134a have been redesigned to disperse a total volume of 25 µl rather than 63 µl when CFCs are used. This modification is the cause of differences in particle size distribution, since this formulation produces smaller particles[1,48] than the previous one containing CFCs. This does not, however, imply a heavier deposition in the respiratory tree, because particles which are too small tend to be discharged with exhalation or to deposit mainly in the alveoli[12].

Table VII shows a comparison of fine particle mass (sum of salbutamol sulphate deposited on stages 2 through 6 of the cascade impactor) of MDIs containing different propellants[49].

The first MDI (HFA and salbutamol) proved as effective as an MDI containing CFCs[50], and was followed by others containing bechlomethasone, fluticasone propionate, triamcinolone acetonide, salmeterol, fenoterol, ipratropium bromide, fenoterol+ipratropium and nedocromil sodium, many of which are at an advanced stage of development[44-59].

Table VI. Sealed lip technique.

1. Remove the mouthpiece cover
2. Shake the MDI energetically
3. If it is a new device, carry out three blank tests making sure you shake the canister well between one actuation and the next
4. Turn the device upside down (mouthpiece facing down)
5. Hold the mouthpiece in your teeth
6. Seal your lips around the mouthpiece
7. Breathe out slowly and thoroughly through the mouthpiece
8. Press the canister bottom and at the same time, breathe in slowly and deeply
9. Hold your breath for approximately 10 seconds
10. Remove the device from your mouth
11. Breathe quietly at your normal rate
12. If prescribed by your physician, wait one minute before repeating the inhalation procedure from 2 to 11
13. Regularly check that the delivery outlet and the mouthpiece are perfectly clean inside and outside

Table VII. Comparison of salbutamol sulphate (Ventolin TM – GlaxoWellcome) fine particle mass (FPM) after delivery from MDIs containing HFA134a and CFCs as propellants.

Metered dose inhaler	*FPM (mg)*
HFA 134a	41[44-45]
CFC Ventolin™	44[44-45]

The surfactants currently available cannot be used with P-134a and P-227 because of their limited solubility in these propellants. Therefore, simple replacement of CFCs with P-134a and P-227 is by no means simple, because of the different physical and chemical properties of these propellants (Table VIII).

Although P-134a could be a valid alternative to CFCs, its reformulation has proved so complex that pharmaceutical companies have been persuaded to develop alternatives such as precompression pumps or intelligent devices capable of delivering the pure drug in powder form directly[60]. Therefore, the new propellants[9,42-62] appear to be promising alternatives to CFCs, although further clinical, toxicological and particle size studies are necessary, especially in terms of dose consistency in order to assess their real efficacy.

Furthermore, as things now stand, MDI reformulation would appear to be a very complex procedure and one that cannot be used for all drugs.

Propellants such as butane, isobutane and propane have not been shown to be compatible with pulmonary use[60]. Another important problem connected with the use of MDIs is the fact that these devices provide no indication of whether the drug has been inhaled or not and how many doses the device has delivered.

This is the reason behind the development of "Chronolog", a recording system which can be fitted to an MDI canister to determine at what time of the day the inhaler was used and how many doses the patient received each time it was used[63].

The single puff dose delivered with this device does not seem to differ much from the dose delivered when the standard canister holder is used. Consequently, the therapeutic effect of the drug used is unchanged[64].

Breath-actuated metered dose inhalers

The Autohaler system is a new type of metered dose inhaler (breath actuated), releasing the drug during inhalation. This device is likely to increase lung deposition in patients with a poor inhalation technique and contains 60% less CFCs than a traditional metered dose inhaler[35].

Autohaler, which is also available with bechlomethasone in HFA propellant[65], is a metered aerosol equipped with a spring device which once loaded, is actuated by a moderate inspiratory flow (30 L/min on average), consequently delivering the drug dose in the form of aerosol. Table IX contains a few suggestions about how to use the Autohaler properly.

Recently, Easi-Breathe, a new patient-triggered inhaler has been developed. Easi-Breathe is primed when the mouthpiece cover is opened. When the patient brethes in,the mechanism is triggered and a dose is automatically released into the airstream.

The inhaler works on a pneumatic principle.An internal vacuum restrains an operating spring. The vacuum is released by a valve which operates in response to the patients inhalation allowing the spring to fire the canister releasing a dose. It also has an integral mouthpiece cover and can be actuated at an air flow rate of approximately 20 L/min, which is readily achievable by most patients using MDIs.

Table VIII. Physical and chemical properties of aerosol propellants used for MDIs.

Property	*Trifluoromono-fluoroethane*	*Heptafluoro-propane*	*Trichlorofluoro-methane*	*Dichlorodifluoro-methane*	*Dichlorotetra-fluoromethane*
Molecular formula	CF_3CH_2F	CF_3CHFCF_3	CCl_3F	CCl_2F_2	$C_2Cl_2F_4$
Numerical designation	134a	P-227	CFC-11	CFC-12	CFC-114
Molecular weight	102	107	137.4	120.9	170.9
Vapour pressure at 20°C (psgin)	81.0	58.0	-1.8	67.6	11.9
Boiling point	°C -26.5	-17.0	23.8	-29.8	3.8
Liquid density at 25 °C (g/cm^3)	1.20	1.41	1.476	1.311	1.456

Table IX. Correct use of the autohaler.

- Remove the cover
- Lift the lever
- Shake the inhaler energetically
- Exhale
- Insert the mouthpiece between your lips beyond the incisal edge of teeth
- Breathe in slowly and deeply
- Hold your breath for approximately 10 seconds
- Wait one minute and repeat the procedure if required
- Regularly clean the mouthpiece and delivery outlet carefully with a brush

Table X contains a few suggestions about how to use the Easi-Breathe properly.

Spacers: holding chambers, open tube, reverse flow designs

A spacer device is a tube extension to an MDI or a holding chamber with a port at one end to which a metered-dose inhaler (MDI) is attached, a mask or mouthpiece being fitted at the other end.

Patients dispense drugs (one puff at a time) into the spacer and inhale by breathing normally through the mask or mouthpiece. Approximately 35% of adult patients and, in practice, all children have difficulty synchronising actuation of the MDI with inhalation of the aerosol[4].

To improve inhalation technique spacer devices attached to the MDI can help to overcome this difficulty. The use of a spacer reduces both the velocity and the size of the aerosol particles and dispenses with the need for patient co-ordination between actuation of the MDI and inhalation of the aerosol. Moreover spacers have a size-selective function, retaining the non-breathable particles, thus reducing "cold-Freon effect" and drug deposition in the oropharynx, with fewer local side effects from steroid aerosols such as: coughing, hoarseness, throat discomfort and oral candidiasis[41,68].

Table X. Correct use of the Easi- Breathe.

- Shake the inhaler vigorously
- Hold the inhaler upright and open it by folding down the cap which fits over the mouthpiece
- Breath out normally as far as you comfortably can
- Place the mouthpiece in your mouth between your teeth and close your lips firmly around it, but do not bite it. Make sure that your hand is not blocking the airholes
- Breathe in slowly and deeply through the mouthpiece. Don't stop breathing when the inhaler puffs the dose into your mouth. Carry on until you have taken a deep breath
- Take the inhaler out of your mouth and hold your breath for 10 seconds or as long as is comfortable
- Breath out slowly

Using a metal spacer[69], devices made of Terlux™, washing the spacer in detergent without subsequent rinsing[70] or firing several puffs into the spacer[1], can avoid electrostatic charges which decrease drug output from plastic spacers. Rubbing the spacer with a cloth increases the electrostatic charge. In a metal spacer the aerosol half-life is about 30 sec. compared with about 10 sec in a new plastic spacer; a short half-life increases the need for co-ordination between actuation and inhalation. Therefore non-electrostatic spacers deliver a significantly higher dose than plastic spacers. Similarly, firing in a large-volume spacer increases the lung dose in adults by approximately 50%[71].

Several spacers and holding chambers are available. Dose delivery varies considerably depending on design. Some devices (Aerovent, Ace) can be used to deliver aerosols from MDIs to intubated or tracheostomized patients[72].

The most important factors influencing output from MDI plus add-on device are: spacer material and volume; dead space between inlet and outlet; inlet and outlet valve controls, drug formulation, propellants, evaporation rate, and humidity. The inhalation method is also an important variable in the delivery of inhaled drugs. Inhalation from the spacer must be slow and multiple actuations should be avoided because they may reduce drug output from the spacer[73]. Patients should remember to wait a minute between 2 puffs of the inhaler, even when using the spacer. This ensures the prescribed amount of medication.

Certain spacers (Volumatic, Nebuhaler) are designed to fit only a single type of MDI, wherease others can be used with all types. The right kind of spacer must be used, choosing the most suitable kind, ideally, after testing a number of different devices for the individual patient.

Table XI. Types of spacers.

Spacer	Material	Brand	Manufacturer	Volume (ml)
Holding chambers	Plastic	Volumatic	GlaxoWellcome, UK	750
	Plastic	Babyhaler	GlaxoWellcome, UK	350
	Plastic	Aerochamber	Monaghan Medical, USA	145
	Plastic	Nebuhaler	Astra Draco, Sweden	700
Non electrostatic holding chambers	Metal Terlux™	NebuChamber	Astra Draco, Sweden	250
		Fluspacer	Menarini, Italy	305
Open tube	Plastic	Aerovent	Monaghan Medical, USA	145
	Plastic	BI	Boehringer Ingelheim, GR	50
	Plastic	Jet	Chiesi, Italy	103
Reverse flow	Plastic	Ace	DHD, USA	170
	Plastic	Inspirease	Scering Corporation, USA	750
	Plastic	Optihaler	HealthScan, USA	45

Results of several studies indicate that MDIs with spacers are as effective as nebulizers in the treatment of asthma. During an acute attack the use of high dose (10-15 puffs) short-acting β_2 agonist via an MDI and large volume spacer is an effective alternative to its use via a nebuliser β_2 agonist. In addition, cost-analysis studies indicate that for hospitalised adult patients with asthma exacerbations, treatment with either MDIs or nebulizers produce equivalent responses, and MDI use is not associated with longer periods of hospitalisation[74].

Moreover, hydrofluoroalkane, released from the MDI at a lower speed than conventional CFCs, delivers more salbutamol than the conventional formulation when used either with the Aerochamber or Nebuhaler spacer[75] while, in vivo, salbutamol from a CFC-free MDI given via a small volume metal spacer (Nebuchamber) produces significantly greater delivery than from a dry powder inhaler (Turbuhaler)[76]. This data suggests that, in the near future, a reduction in the number of doses should be considered when a CFC-free MDI is used with a spacer, and that new spacers need to be developed for the new HFA metered dose inhaler, to reduce costs and undesired side effects. Table XI lists a number of spacers, with varying sizes and shapes.

Valved spacers (Aerochamber, Fluspacer, Volumatic, Nebuhaler) are generally preferable to smaller spacers and should be used in the following instances: (a) by all adult patients with poor inhaler technique; (b) by children of all ages; (c) children under 4 years of age may use an MDI and a small volume valved spacer (Aerochamber) with a face mask; (d) by all patients using inhaled steroids from MDIs.

The disadvantages of spacers are that they are bulky, and difficult to carry about; in addition, the valves sometimes stick or become otherwise faulty. Table XII contains some suggestions about how spacers should be used properly.

The past 5 years of research[1] have produced technological innovations such as non electrostatic or hypostatic components, devices for limiting flow, systems helping co-ordination between delivery of the drug and inhalation, beeper warnings informing patients that they are inhaling too rapidly, and spacers fitted to mechanical ventilation circuits. Much can still be achieved.

The future of clinical and technological research for the purpose of improving thera-

Table XII. Metered dose inhaler plus spacer: correct inhaler technique.

- Shake the inhaler
- Fix MDI upright in spacer
- Keep lips on mouthpiece or keep face mask tightly applied to face (infants)
- Breathe in and out through spacer
- Fire device while taking 1-2 (adults) or 3-4 (children) slow, deep breaths
- Ensure valve is operating
- Keep spacer clean and dry

peutic response and acceptance of therapy and prescribed devices by patients, will concentrate on highly efficient spacers which are not only easy to use and carry, but also assist the doctor in keeping the illness under control, restricting or suppressing the side effects of drugs, propellants and additives used in dosed aerosols. Technological innovations will turn spacers into "multi-purpose" devices suited to current and future needs, by allowing the progression of the illness to be monitored and the therapy and effectiveness of the inhalation technique prescribed by the doctor to be measured.

Conclusion

The purpose of the Montreal international agreement[77], according to which the production of CFCs should be discontinued, is to protect the environment by preventing further damage to the ozone layer. This critical goal, however, should not endanger the health of patients suffering from bronchial asthma and COPD and using metered aerosols to treat their condition.

The proposed use of alternative propellants to CFCs (such as HFAs) should therefore guarantee at least the same level of efficacy and safety for the patients as currently used delivery systems, the same drug availability, and, if possible, new and better inhalers. To achieve these aims, pharmaceutical companies are researching effective alternatives.

Some of the results appear to be highly interesting although further (especially long-term) research is required to guarantee the safety of these new CFC-free devices.

Training programs targeted on both health-care workers and patients are also recommended, to teach the proper use of these devices, and, in addition, to explain the therapeutic and environmental advantages, if any, arising from a shift to new drugs and delivery systems.

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