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A comparison of drug delivery from a metered-dose inhaler plus an inspiratory flow control device with a metered-dose inhaler plus a spacer device

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Metered-dose inhalers (MDIs) deliver medication directly to the airways and thus reduce systemic effects without compromising the desired response. Problems with patient compliance exist, and there is concern about whether a therapeutic dose reaches the airways.¹ Slower inspiratory flow rates (400 to 500 ml/sec) for delivering aerosol medication may be better than rapid (1300 ml/sec) flow rates.² A device that controls inspiratory flow rate at 500 or 700 ml/min has been introduced. This study evaluates pulmonary albuterol delivery by this device and compares it with a standard spacer device that is known to enhance MDI efficacy.³

METHODS

Five volunteers without lung disease used both devices. They were trained to use an MDI with an inspiratory flow control device (IFCD), which can be set to maintain inspiratory flow at about 500 or 700 ml/min (MistAssist; Ballard Medical Products, Draper, Utah) and with a commonly used spacer device (Aero-chamber; Monaghan Medical Corp., Plattsburgh, N.Y.). On different days, 30 minutes after drinking 500 ml of water, subjects used either the IFCD or the spacer device with an albuterol MDI and inspired four inhalations of 100 µg of albuterol. After a normal expiratory maneuver to approximately the functional residual capacity level, the mouthpiece of the IFCD or the spacer device was placed between the lips. With the spacer device the MDI was actuated, and the subject inspired the mist in the

Abbreviations used

IFCD: Inspiratory flow control device
MDI: Metered-dose inhaler

chamber until total lung capacity was reached. With the IFCD the subject set inspiratory flow at 700 ml/min and inhaled. When the indicator ball reached the top of the device, the MDI was actuated while the subject continued to inspire until total lung capacity was reached. The end of the mouthpiece of the IFCD is 9 cm from the point of delivery of the MDI. Subjects held their breath at total lung capacity for 10 seconds with both devices and then exhaled slowly. This was repeated for all inhalations with each device. Inhalations were performed at 30-second intervals. Instructions provided with the two devices were followed. Thirty minutes later, urine was collected; the volume was measured and then frozen and stored at -20° C.

Unmetabolized urine albuterol was measured by high-pressure liquid chromatography with the method of Hindle and Chrystyn.⁴ This was performed by National Medical Services, Inc. (Willow Grove, Pa.). This is representative of pulmonary albuterol delivery.^{4,5} A previous study has shown that there is very little absorption of albuterol in the oral cavity.⁶ Comparisons were made by using a paired *t* test.

RESULTS

There were five participants, all healthy lifelong non-smokers: four male subjects ages 13, 15, 45, and 46 years and one 43-year-old woman. Table I presents the results. In each participant the IFCD set at 700 ml/min resulted in more unmetabolized urinary albuterol ($p = 0.011$). The increases with the IFCD when compared with the spacer device ranged from 6.26% to 63.55% more urinary albuterol in these five participants.

DISCUSSION

This study demonstrates that an IFCD set at 700 ml/min during albuterol delivery from an MDI increases

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Mr. Dwork, the developer of MistAssist, has transferred all rights to Ballard Medical Products, Draper, Utah 84020 and thus, still has a financial interest in the product. Neither Dr. Kanner nor Dr. Kanter has any financial interest whatsoever in MistAssist.

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TABLE 1. Urine albuterol recovered 30 minutes after medication delivery in five healthy participants using an MDI with either an IFCD or a spacer device

Participant	Albuterol in urine (ng)		Percent increase with use of IFCD
	IFCD	Spacer device	
1	16,240	11,500	41.2
2	16,960	15,960	6.3
3	11,600	7,200	61.1
4	26,680	20,740	28.6
5	7,360	4,500	63.6
Mean*	15,768	11,980	
SD	7,224.7	6,550.0	

* $p = 0.011$ for comparison of urinary albuterol when using the IFCD versus the spacer device.

the pulmonary deposition of drug when compared with a standard spacer device. It is possible that an IFCD setting at 500 ml/min would further improve drug delivery. The increased dose delivered to the lungs might cause adverse side effects; and if such side effects are noted, a downward dose adjustment must be made. An important potential benefit is that the IFCD could result in administration of less drug, providing an equal effect and a reduction in medication costs.

Hindle and Chrystyn⁴ and Hindle et al.⁵ have shown that unmetabolized urinary albuterol in the first 30 minutes after drug inhalation is an indication of pulmonary drug delivery. Inter-subject variability in the amount of urinary albuterol, measured 30 minutes after inhalation, may have several causes. These include differences in lung volume at the time of MDI actuation, differences in inspiratory flow when the spacer device is used (including the possibility that the patient might spontaneously inhale the drug from the spacer device at 500 to 700 ml/min), differences in the

amount of air inspired during drug delivery caused by differences in lung size, and differences in renal drug clearance between subjects. However, in all five subjects the IFCD proved superior to the spacer device. The subjects were healthy and were trained before data collection. Thus the devices require study under clinical conditions.

In summary, an IFCD set at 700 ml/min proved superior to a spacer device in delivering medication from an MDI to the lungs of healthy participants. Although further clinical studies are needed in patients, this device offers promise for reducing the amount of medication needed for a therapeutic effect in patients with airway diseases, and use of this device might reduce the annual cost of these medicines.

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Food allergy to Belgian endive (chicory)

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Belgian endive (*Cichorium intybus*) also called chicory, witloof, or chicon is a common salad plant or vegetable in Europe belonging to the family of Asteraceae (Compositae). Foods of the Asteraceae family such as lettuce,

Abbreviations used

DBPCFC: Double-blind, placebo-controlled food challenge
SDS-PAGE: Sodium dodecylsulfate-polyacrylamide gel electrophoresis

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artichoke, dandelion, or oyster plant are rarely reported to cause hypersensitivity.¹⁻³ On the other hand, mugwort in Europe and short and giant ragweed in the United States, both wind-pollinated plants of this family, are well-known causes of respiratory allergy. Foods that are most com-