Evaluation of Aerosol Drug Output from the OptiChamber™ and AeroChamber® Spacers in a Model System

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ABSTRACT
Metered-dose inhalers (MDIs) are an effective means of generating drug-containing aerosols targeted for delivery to intrapulmonary airways. Many problems associated with incorrect patient use of MDIs are mitigated by adding a valved spacer device to the inhaler mouthpiece. This in vitro study compared the efficiency of drug output through a new spacer device, OptiChamber™ (HealthScan Products Inc., Cedar Grove, NJ), to that of a device commercially available since the 1980s, AeroChamber® (Monaghan Medical, Plattsburgh, NY). Testing utilized MDI formulations of albuterol, beclomethasone dipropionate, and cromolyn sodium. OptiChamber equaled or, in the majority of cases, exceeded AeroChamber in output of the three drugs at two simulated inspiratory flow rates. Drug output from OptiChamber was found to be less sensitive to changes in flow rate than that from AeroChamber. OptiChamber also showed less decrease in drug output than AeroChamber when time delays were introduced between MDI actuation and the start of a simulated inhalation. Mass median aerodynamic diameters of drugs exiting the two spacers were generally similar to those of drugs exiting the MDI alone. However, spacers were shown to nearly eliminate the output of large-size drug particles (>5.8 μm), which can result in oropharyngeal drug deposition. Emitted fine-particle drug (<5.8 μm) doses from OptiChamber were greater than those from
INTRODUCTION

Therapeutic aerosols are widely used in the treatment of reversible airway obstruction and parenchymal disease. Pressurized metered-dose inhalers (MDIs) are a convenient, portable means of respiratory drug delivery. When used correctly, MDIs deliver a greater percent of the metered dose to the lower respiratory tract than other forms of clinical aerosol generators (e.g., jet nebulizers, dry powder inhalers) (1). However, poor inhalation technique, leading to highly variable drug deposition, is a common problem with patients using MDIs (2). When coordination of MDI canister actuation with inhalation is a concern, valved spacers and breath actuated inhalers (BAIs) (e.g., Autohaler®, 3M Riker, St. Paul, MN) have proven beneficial. BAIs may alleviate the coordination issue, but do not provide the additional benefits of a valved spacer. The use of a spacer attached to the MDI allows for particle deceleration and mean particle size reduction of the inhaled drug by increasing propellant evaporation. These combine to minimize oropharyngeal drug deposition (which in the case of steroid aerosols also reduces unwanted side effects such as oral candidiasis) (3). The net result is increased drug deposition in intrapulmonary airways with resulting greater therapeutic efficiency (4).

There have been few comparisons of the relative efficacy of different commercially available spacers. One common index of spacer function is fine-particle dose output measured under ideal use conditions. The United States Pharmacopeia defines fine-particle dose as particles under 5.8 μm in size. However, patient timing and technique remain significant, but ill-defined obstacles to the maximization of spacer benefits. A pilot study demonstrated delays between canister actuation and the start of inhalation may be as great as 12 sec (5). This study tested the hypothesis that improved spacer design might reduce the variability caused by: (1) varying inhalation delay (time between MDI canister actuation and start of inspiration); and (2) inspiratory flow rate. Aerosol testing compared OptiChamber, a new MDI spacer, with AeroChamber, another valved holding chamber, and with an MDI alone. The devices were compared with respect to: (1) total drug output at two simulated inspiratory flow rates; (2) average drug particle size delivered; and (3) the effect of inhalation time delay.

Each comparison utilized three medical aerosols currently commercially available in MDI form: albuterol (Ventolin®, Allen & Hanburys, Division of Glaxo Inc., Research Triangle Park, NC), beclomethasone dipropionate (Beclovent®, Allen & Hanburys, Division of Glaxo Inc., Research Triangle Park, NC), and cromolyn sodium (Intal®, Rhone-Poulenc Rorer, Collegeville, PA).

MATERIALS AND METHODS

Test Equipment

Both OptiChamber and AeroChamber spacers are clear, cylindrical chambers whose principal difference is size (OptiChamber, 4.6 cm ID × 13 cm; AeroChamber, 4.2 cm ID × 10.5 cm). Each has a mouthpiece on one end and a flexible, elastomeric MDI actuator adapter on the other. Silicon flap valves near the mouthpiece prevent patient exhalation into the spacer.

MDIs with or without spacer devices were attached to two types of collection devices for testing. A horizontal glass filter assembly (Fisher Scientific, St. Louis, MO) was used to determine total drug output (from the mouthpiece) exiting the spacers. An Andersen eight-stage, nonviable cascade impactor (1 ACFM Cascade Impactor) was used to determine the
particle size, measured as mass median aerodynamic diameter (MMAD) of the aerosolized drugs exiting the spacers. Each test apparatus was connected to a regulated vacuum line capable of maintaining a constant air flow typical of a patient inhalation. Specific delays between actuation of the MDI and the initiation of air flow could also be achieved. Drug was recovered from the filter or cascade impactor in an appropriate solvent, and the concentration determined via high-performance liquid chromatography with spectrophotometric detection.

Protocol

Each MDI canister (albuterol, 90 μg/actuation; beclomethasone dipropionate, 42 μg/actuation; cromolyn sodium, 800 μg/actuation) was shaken for 15 sec prior to each actuation into the spacer/collection device. Total drug output (average of 5 replicate MDI actuations) and MMAD (following 10 replicate MDI actuations) from the mouthpiece of OptiChamber or AeroChamber were determined at a simulated inspiratory flow rate of 28 L/min. Total drug output was also determined at 55 L/min. Measurements were made using the same MDIs without spacers. Finally, the effect of inhalation delay on total drug output was determined at a simulated inspiratory flow rate of 55 L/min for each spacer.

RESULTS

Both spacer devices tested reduced the total amount of drug emitted from the mouthpiece compared to the MDI alone (Fig. 1a–c). OptiChamber and AeroChamber increased the percentage of emitted drug present as fine particles compared to the MDI alone (Fig. 2). For each of the three drugs tested at a flow rate of 28 L/min, OptiChamber provided significantly (p < 0.05) more total drug (Fig. 1) and more drug emitted as fine-particle dose than AeroChamber (Fig. 3). At a flow rate of 55 L/min, the drug output from OptiChamber was the same as or more than that from AeroChamber with or without the presence of a time delay between canister actuation and the start of a simulated inhalation (Fig. 4a–c).

For AeroChamber, the variation in albuterol exiting the spacer at different flow rates (percent difference in total dose exiting the spacer at 28 L/min vs. 55 L/min) was 42% compared to 2% variation for OptiChamber. The variation in beclomethasone exiting the spacer was 50% for AeroChamber versus 31% for OptiChamber and the variation in cromolyn sodium exiting the spacer was 94% for AeroChamber versus 58% for OptiChamber (Fig. 1a–c). The MMADs of drugs exiting the two spacers were generally similar to those exiting the MDI alone. However, spacers were shown to nearly eliminate the output of drug particles >5.8 μm. It can be concluded that, due to its slightly larger size, OptiChamber’s drug output was less sensitive to variation in inspi-
Figures 2, 3, and 4 show the percentage of emitted drug present as fine particles (<5.8 μm) for Albuterol, Beclomethasone, and Cromolyn sodium, respectively.

**CONCLUSIONS**

Spacers were shown to reduce the amount of drug exiting the MDI mouthpiece. This dose reduction became increasingly more pronounced with increased delay time between MDI actuation and simulated inhalation. Nevertheless, as expected, in the absence of a delay, addition of a spacer to the MDI greatly reduced the output of large drug particles normally destined for deposition in the mouth and throat.

Spacers have been shown to improve forced expiratory volume in 1 sec (FEV₁) in adult asthma patients using bronchodilators (6). The present study represents a functional comparison of two spacer devices. Although similarly designed, OptiChamber’s slightly larger diameter and longer unobstructed path length encountered by the aerosol spray (combining to yield 50% greater volume) appears to raise its overall in vitro output performance above that of AeroChamber.

OptiChamber delivered as much or more fine-particle drug dose and was less sensitive to inspiratory flow rate and inhalation time delays than AeroChamber. These findings suggest that use of OptiChamber can lead to reduced variability in the aerosol dose inhaled by patients.

It is inappropriate to assume that all valved holding spacers function as efficient holding chambers. Holding chambers with volumes...
of approximately 750 ml are likely to retain airborne particles more efficiently than similarly designed devices having significantly smaller volumes. The results of the time delay experiments further encourage efforts to revise the National Asthma Education and Prevention Program guidelines (7), which advocate using spacers as 3–5 sec holding devices. Sensitivity of drug output to inhalation delays should be evaluated by spacer manufacturers. Additional functional comparisons of commercially available spacers are needed to ensure that the public has access to spacers providing consistent output under a wide range of patient use conditions.

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