The Importance of Nonelectrostatic Materials in Holding Chambers for Delivery of Hydrofluoroalkane Albuterol

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INTRODUCTION: Electrostaticattraction of aerosolized particles to the inner walls of an aerosol holding chamber (HC) made from a nonconducting material can reduce medication delivery, particularly if there is a delay between actuation and inhalation. OBJECTIVE: Compare total emitted mass and fine-particle mass (mass of particles < 4.7 μm) of hydrofluoroalkane-propelled albuterol from similar-sized HCs manufactured from conductive material (Vortex), charge-dissipative material (AeroChamber Max), and nonconductive material (OptiChamber Advantage, ProChamber, Breathrite, PocketChamber, and ACE), with and without wash/rinse pretreatment of the HC interior with ionic detergent, and with 2-s and 5-s delays between actuation and inhalation. METHODS: All the HCs were evaluated (1) directly from their packaging (with no wash/rinse pretreatment) and (2) after washing with ionic detergent and rinsing and drip-drying. We used an apparatus that interfaced between the HC mouthpiece and the induction port of an 8-stage Andersen cascade impactor to simulate a poorly coordinated patient, with delays of 2 s and 5 s between actuation and inhalation/sampling, at 28.3 L/min. RESULTS: With the 2-s delay, the delivered fine-particle mass per actuation, before and after (respectively) wash/rinse pretreatment was: AeroChamber Max: 23.8 ± 4.8 μg, 21.5 ± 3.2 μg; Vortex: 16.2 ± 1.7 μg, 15.5 ± 2.0 μg; OptiChamber Advantage: 2.6 ± 1.2 μg, 6.7 ± 2.3 μg; ProChamber: 1.6 ± 0.4 μg, 5.1 ± 2.5 μg; Breathrite: 2.0 ± 0.9 μg, 3.2 ± 1.8 μg; PocketChamber: 3.4 ± 1.6 μg, 1.7 ± 1.6 μg; ACE: 4.5 ± 0.9 μg, 5.4 ± 2.9 μg. Similar trends, but greater reduction in aerosol delivery, were observed with the 5-s delay. Significantly greater fine-particle mass was delivered from HCs made from conducting or charge-dissipative materials than from those made from nonconductive polymers, even after wash/rinse pretreatment ($p < 0.01$). The fine-particle mass was also significantly greater from the AeroChamber Max than from the Vortex, irrespective of wash/rinse pretreatment or delay interval ($p < 0.01$). CONCLUSION: HCs made from electrically conductive materials emit significantly greater fine-particle mass, with either a 2-s or 5-s delay, than do HCs made from nonconducting materials, even with wash/rinse pretreatment. *Key words: aerosol, holding chamber, fine-particle mass.* [Respir Care 2006;51(5):503–510. © 2006 Daedalus Enterprises]

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The study was funded by Monaghan Medical Corporation. The study was performed at the Aerosol Research Laboratory of Trudell Medical International, London, Ontario, Canada.

Joseph L. Rau is a speaker and consultant for Monaghan Medical Corporation, an affiliate of Trudell Medical International.

Joseph L Rau PhD RRT FAARC presented a version of this paper at the International Conference of the American Thoracic Society, held May 20–25, 2005, in San Diego, California.

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Introduction

Pressurized metered-dose inhalers (pMDIs) have been a convenient, low-cost, and portable means of delivering aerosolized medication for more than 50 years. However, good inhaler technique can be difficult to achieve,[1–2] and valved holding chambers (HCs) are prescribed to address the issue of actuation/inhalation coordination and to remove the ballistic fraction of the pMDI aerosol plume, which comprises mainly larger particles that would otherwise deposit on the oropharynx.[3–4] HCs also retain the finer particles in suspension for some time after inhaler actuation; thus those particles are available to be inhaled.[5]

Despite the advantage of being able to contain the aerosol in an HC, delayed inhalation has also been associated with significant loss of medication in laboratory simulations.[6] Manufacturers' instructions recommend inhaling while actuating the pMDI, but many patients have imperfect coordination,[1–2] which can lead to delay between actuation and inhalation from the HC. An important cause of aerosol-particle loss, in addition to the losses associated with gravitational settling, appears to be the adhesion of particles to the HC's inner surface, caused by electrostatic charge inside the HC. HCs are manufactured from nonconducting materials such as polycarbonate or polyester,[7] which acquire surface electrostatic charge during manufacture and use.[8] The loss of airborne particles caused by electrostatic attraction to the interior surface of an HC is a rapid and continuous process, so the aerosol half-life within the device is significantly reduced.[9] Wildhaber et al reported a 40% reduction in albuterol particles $< 6.8\ \mu m$ from a large-volume polycarbonate HC that had not been subjected to wash/rinse pretreatment,[8] and in a separate study up to 70% increase in fine-particle delivery from nonconducting HCs by washing with detergent, followed by drip-drying.[10]

Recent in vitro studies have shown that electrostatic charge is more prevalent with some of the new hydrofluoroalkane (HFA)-propelled formulations intended as replacements for their chlorofluorocarbon predecessors.[11–13] Manufacturers therefore generally instruct users to wash and dry HCs before use in order to mitigate charge-related loss of medication.[5] The need to prewash an already clean device complicates its use.

Recently, 2 new small-volume HCs constructed of electrostatic-charge-dissipative or conducting materials have become available in the United States marketplace. The Vortex (PARI Respiratory Equipment, Midlothian, Virginia) is manufactured from an electrically conducting and opaque aluminum-bodied chamber, although inhalation-valve operation can be observed through a transparent end-cover. The AeroChamber Max (Monaghan Medical, Plattsburgh, New York) is a similar-sized, transparent-bodied chamber constructed from a proprietary charge-dissipative polymer that allows observation of the aerosol-plume generation and valve operation. Charge-dissipative polymers behave similarly to electrically conductive surfaces and both can be termed "nonelectrostatic."

The purpose of the present study was to compare total emitted mass (TEM) and fine-particle mass (FPM) (mass of the particles $< 4.7\ \mu m$) of albuterol (Ventolin-HFA) from the Vortex and AeroChamber Max, versus 5 HC models of similar size made with nonconductive materials, with and without wash/rinse pretreatment, and with 2-s and 5-s inhalation delays.

Methods

Table 1 lists the HCs we evaluated (5 HCs per test group, 1 measurement per device). We chose Ventolin-HFA (GlaxoSmithKline, United Kingdom, 108 μg albuterol sulfate, equivalent to 90 μg albuterol base emitted from the actuator mouthpiece) as a representative HFA-formulated bronchodilator that is widely available in North America. All the HCs were initially tested without pretreatment (ie, directly out of the packaging) to simulate use in an emergency situation, when time to prewash the device is unavailable. Each HC was subsequently retested, after following the manufacturer's United States instructions to pretreat by washing in mild ionic detergent (Sunlight, Unilever, Canada), followed by rinsing in clean water and drip-drying.

An Andersen 8-stage cascade impactor (Thermo Electron, Franklin, Massachusetts) equipped with a United States Pharmacopeia (USP) induction port was operated at 28.3 L/min $\pm$ 5%, in accordance with the procedure described in Chapter 601 of the USP,[14] but with the following modification. A purpose-built delay apparatus containing a solenoid-operated shutter was located at the entry to the induction port.[15] During testing the mouthpiece of the HC was inserted into a tight-fitting recess on the distal side of the delay apparatus such that its exit was located adjacent to the shutter, and the body of the HC was aligned horizontally on-axis with the induction-port entry (Fig. 1).

While the shutter was in the closed position, air could be drawn into the impactor via a narrow slit located on the near side of the shutter, facing the induction-port entrance, without disturbing aerosol contained in the HC. Actuation of the primed pMDI into the HC was detected by a microphone located close by. The microphone signal started the timer, which, after the pre-set 2.0-s or 5.0-s delay, triggered the solenoid that opened the shutter. The movement of the shutter was in the vertical plane and therefore did not disturb the aerosol in the HC. Immediately upon the opening of the shutter, the particles that were still airborne in the HC were drawn, at a constant flow rate and in the horizontal direction, through the induction port and into the impactor. With each HC, 5 actuations were deliv-

Table 1. Holding Chambers Studied in This Investigation

Holding Chamber	Manufacturer	Electrical Properties	Volume (mL)
AeroChamber Max	Monaghan Medical, Plattsburgh, New York	Nonelectrostatic	198
Vortex	PARI Respiratory Equipment, Midlothian, Virginia	Nonelectrostatic	194
OptiChamber Advantage	Respironics HealthScan, Cedar Grove, New Jersey	Nonconducting	218
ProChamber	Respironics HealthScan, Cedar Grove, New Jersey	Nonconducting	155
Breathrite	Ventlab, Mocksville, North Carolina	Nonconducting	125
PocketChamber	Ferraris Respiratory, Orchard Park, New York	Nonconducting	110
ACE	DHD Healthcare, Wampsville, New York	Nonconducting	150

ered, at 30-s intervals, with the same 2-s or 5-s delay, and with shaking of the pMDI canister for 5 s immediately before each actuation. Flow through the impactor was continued for 30 s after the last actuation, then flow was discontinued and the HC was removed from the delay apparatus. Measurements took place at room ambient conditions of 22–23°C and 34–66% relative humidity.

The particulate collected within the HC, the induction port, all the impactor stages, and the impactor's back-up filter was subsequently recovered via elution in known volumes of methanol (100% volume/volume), and the mass of albuterol was measured via high-performance liquid chromatography ultraviolet spectrophotometry (Star System, Varian Associates, Walnut Creek, California) at a detection wavelength of 276 nm.

Comparative measures of FPM of albuterol per actuation emitted from the HC mouthpiece were chosen as an in vitro measure indicative of pulmonary deposition, based on the likelihood that the fine particles penetrate beyond the oropharynx and could serve as a basis for interpreting future clinical studies.[16] FPM was calculated as the cumulative mass that collected on impactor stages 3 through 7 and the impactor's back-up filter (these stages represent the particles < 4.7 μm aerodynamic diameter).[14] The fine-particle fraction (FPF) was also calculated at each condition as the ratio (FPM/TEM) $\times$ 100, in which TEM is the total emitted mass of albuterol per actuation emitted from the HC mouthpiece.

Statistical analyses were performed using statistical software (Systat 7.0, SPSS, Chicago, Illinois). An overall comparison of the HCs and time delays was performed with a split-plot, repeated-measures analysis of variance.[17] Follow-up comparisons were made using Tukey's honest significant difference test and Tukey's ratio with the q statistic,[17] as well as with a paired Student's t test with Bonferroni adjustment of probabilities. Differences were deemed significant when the probability (p) of falsely rejecting the null hypothesis was < 0.05.

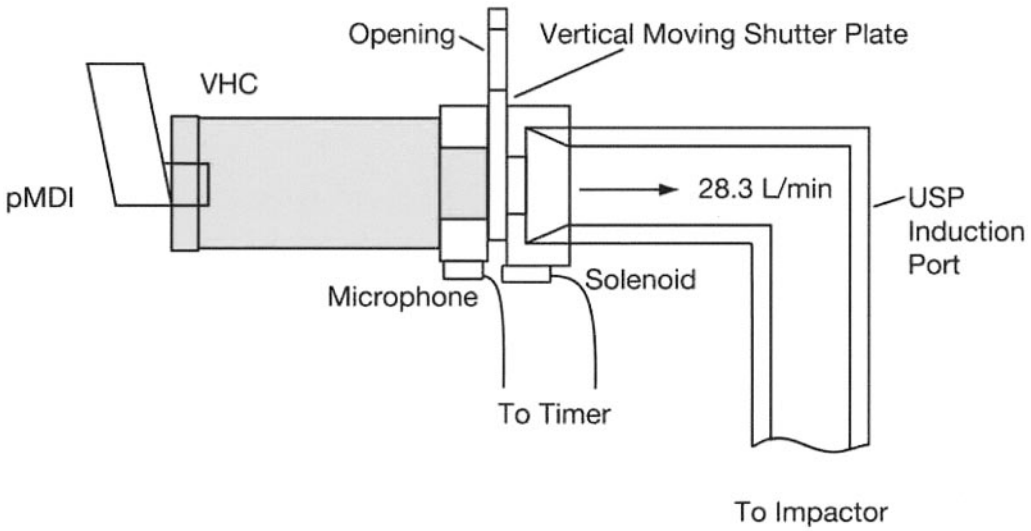

Fig. 1. Configuration of the pressurized metered-dose inhaler (pMDI), valved holding chamber (VHC), delay apparatus (shutter, microphone, and timer), and United States Pharmacopeia (USP) induction port of the cascade impactor sampling system.

Table 2. Total Emitted Mass and Fine-Particle Mass With No Wash/Rinse Pretreatment of the Holding Chamber*

Holding Chamber	Delay			
	2 seconds		5 seconds	
	TEM (mean ± SD μg/actuation)	FPM (mean ± SD μg/actuation)	TEM (mean ± SD μg/actuation)	FPM (mean ± SD μg/actuation)
AeroChamber Max	26.3 ± 5.2	23.8 ± 4.8	21.2 ± 2.5	19.1 ± 2.1
Vortex	17.3 ± 1.8	16.2 ± 1.7	13.5 ± 1.6	12.7 ± 1.4
OptiChamber Advantage	2.9 ± 1.2	2.6 ± 1.2	1.0 ± 0.1	1.0 ± 0.1
ProChamber	1.8 ± 0.4	1.6 ± 0.4	1.0 ± 0.5	0.9 ± 0.5
Breathrite	2.1 ± 0.9	2.0 ± 0.9	0.6 ± 0.4	0.5 ± 0.5
PocketChamber	3.4 ± 1.6	3.4 ± 1.6	1.0 ± 0.7	1.0 ± 0.7
ACE	4.9 ± 1.0	4.5 ± 0.9	3.4 ± 0.9	3.2 ± 0.8

*n = 5 devices/group
TEM = total emitted mass
FPM = fine particle mass (particles < 4.7 μm)

Table 3. Total Emitted Mass and Fine-Particle Mass With Wash/Rinse Pretreatment of the Holding Chamber*

Holding Chamber	Delay			
	2 seconds		5 seconds	
	TEM (mean ± SD μg/actuation)	FPM (mean ± SD μg/actuation)	TEM (mean ± SD μg/actuation)	FPM (mean ± SD μg/actuation)
AeroChamber Max	23.3 ± 3.8	21.5 ± 3.2	19.9 ± 1.6	18.6 ± 1.8
Vortex	16.3 ± 2.2	15.5 ± 2.0	12.1 ± 3.2	11.4 ± 2.7
OptiChamber Advantage	7.1 ± 2.5	6.7 ± 2.3	2.4 ± 1.4	2.3 ± 1.3
ProChamber	5.5 ± 2.6	5.1 ± 2.5	1.7 ± 0.3	1.5 ± 0.3
Breathrite	3.2 ± 1.8	3.2 ± 1.8	0.4 ± 0.4	0.4 ± 0.4
PocketChamber	1.7 ± 1.6	1.7 ± 1.6	0.4 ± 0.5	0.4 ± 0.5
ACE	5.6 ± 3.0	5.4 ± 2.9	3.0 ± 1.5	2.9 ± 1.4

*n = 5 devices/group
TEM = total emitted mass
FPM = fine particle mass (particles < 4.7 μm)

Results

Values of TEM and FPM, without and with wash/rinse pretreatment, are summarized in Tables 2 and 3, respectively. The total mass recovered was within ±25% of label claim (90 μg/actuation) for all the measurements. Both TEM and FPM from the nonelectrostatic AeroChamber Max and Vortex HCs significantly exceeded the equivalent values from all the nonconducting devices, with each time delay, irrespective of wash/rinse pretreatment (via Tukey's ratio with the q statistic, $p < 0.01$). The higher drug output was associated with lower retention of albuterol within these HCs with the 2-s delay and no wash/rinse pretreatment (Fig. 2). Similar trends were obtained with the 2-s delay and wash/rinse (Fig. 3). Comparing the nonelectrostatic devices, the AeroChamber Max delivered significantly more medication than did the Vortex, with or without wash/rinse, and at both delays ($p < 0.01$).

Wash/rinse appeared to result in small increases in FPM with two of the nonconducting HCs (OptiChamber Advantage and ProChamber). These increases were more evident with the shorter delay interval, with which higher mass output values were obtained. However, this effect was significant only with the OptiChamber Advantage (2.6 ± 1.2 μg/actuation, vs 6.7 ± 2.3 μg/actuation with 2-s delay, $p = 0.028$ via a paired Student's t test with Bonferroni adjustment). There was no difference in FPM values between the 2 nonelectrostatic HCs with or without wash/rinse ($p > 0.05$ via paired Student's t test with Bonferroni adjustment).

There were small decreases in FPM associated with increasing the delay from 2 s to 5 s, but these decreases were statistically significant only with the Vortex, ProChamber, and PocketChamber without wash/rinse, and with the OptiChamber Advantage with wash/rinse ($p < 0.05$ via paired t test with Bonferroni adjustment, for each HC).

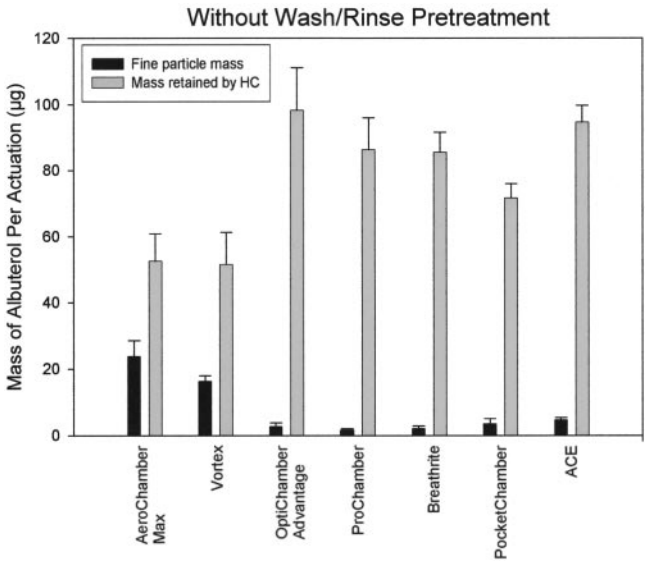

Fig. 2. Emitted fine-particle mass (FPM) and drug mass retained within the holding chambers (HCs), with a 2-s delay between actuation of the pressurized metered-dose inhaler (pMDI) and beginning of flow for impactor sampling, tested without wash/rinse pretreatment of the HCs.

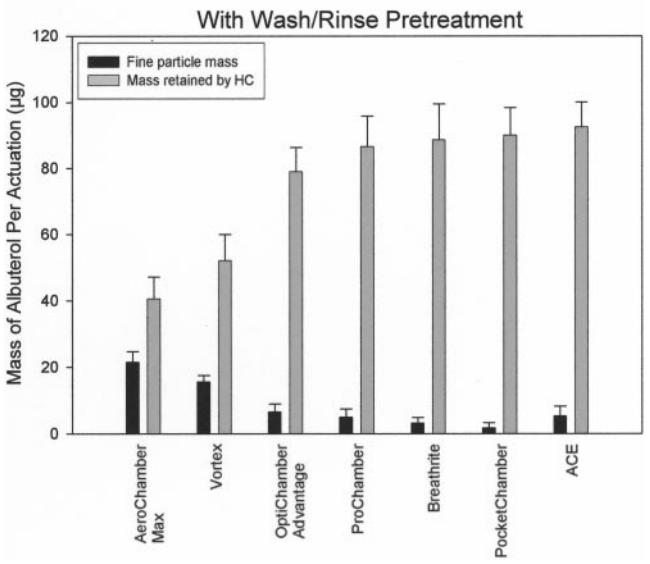

Fig. 3. Emitted fine-particle mass (FPM) and drug mass retained within the holding chambers (HCs), with a 2-s delay between actuation of the pressurized metered-dose inhaler (pMDI) and beginning of flow for impactor sampling, tested with wash/rinse pretreatment of the HCs.

Discussion

Our study highlights the large performance differences between these small-volume HCs. The influence of delay on delivery of medication is partly responsible for the reduced FPM and TEM, in comparison with no delay. Gravitational sedimentation occurs as a continuous process of aerosol-particle removal within the HC, so drug output is expected to decrease with a longer delay.[9] Imposing a delay between actuation and sampling, to simulate use by uncoordinated patients, who are frequently prescribed HCs, is an important difference that distinguishes our investigation from studies in which HC pretreatment was examined without simulation of delayed inhalation,[18] or in which a time delay was not specified.[8,19] The USP method for evaluating HCs does not incorporate a delay,[14] so USP-method testing may give an unrealistically optimistic picture of HC performance. The need to more closely simulate use by the poorly coordinated patient resulted in a recommendation to incorporate a 2-s delay between actuation and sampling for part of the in vitro evaluation of spacers and HCs in a recently introduced Canadian standard that was developed with guidance from clinicians.[20]

Laboratory studies in which delay was simulated are useful to illustrate the magnitude of HC aerosol loss. For instance, Dalby et al[21] conducted a laboratory investigation in which they sampled albuterol and beclomethasone dipropionate delivered via the OptiChamber (predecessor to the OptiChamber Advantage) at 55 L/min to a filter collection system, and they found that a 2-s delay decreased TEM by approximately 25% with albuterol and 40% with beclomethasone. The corresponding losses when the delay was increased to 5 s were approximately 70% and 55%.

Childers et al,[6] sampling at 28.3 L/min with a cascade impactor and a USP induction port, observed reduced delivery of flunisolide and beclomethasone dipropionate particles < 5.8 μm aerodynamic diameter with a 5-s delay with 4 small HCs manufactured from nonconducting materials, and the decrease in FPM was similar to that reported by Dalby et al.[21]

Furthermore, Wildhaber et al[10] found that the delivery of albuterol particles < 6.8 μm aerodynamic diameter decreased significantly, from 33% to 12% of the mass that exited the pMDI metering valve, when they simulated a 5-s delay with a small-volume, nonconducting HC.

Finally, O'Callaghan et al,[22] in a more extreme example of extended delay simulation, showed that imposing a 20-s interval between actuation and inhalation from a nonconducting HC caused a 67% decrease in sodium cromoglycate particles < 5 μm aerodynamic diameter.

Dalby et al,[21] Childers et al,[6] and Wildhaber et al[10] examined HC performance with delay-times that are more comparable to the delay intervals we chose for the present investigation, and also to the duration of delay likely to be seen with poor patient coordination.[23]

The effect of delayed inhalation on HC performance has also been examined with breathing simulators, although such methodology only permits measurement of TEM rather than FPM, because simultaneous particle-size anal-

ysis is not easily carried out.[24] Wilkes et al[25] evaluated a number of add-on devices, including 5 different types of small-volume nonconducting HC, using a lung-model simulation of adult tidal breathing, with a 1-s delay between actuation and inhalation. Prior to testing, the HCs were each given 5 actuations of albuterol to coat (prime) the interior surfaces with medication. The results of this study were inconclusive, because TEM (expressed as a percentage of nominal dose) declined with two of the HCs, but remained comparable with the others. However, as well as the probable reduction in electrostatic charge caused by preconditioning the interior surfaces with medication, the relatively short delay they used may also have contributed to their variable results. It is not clear how the emitted FPM compared with and without delay, because this group made these measurements in a parallel study with cascade impactor with no delay.

The presence of electrostatic charge also exacerbates the loss of medication in an HC.[8–10,19] Drug output increases when a nonconducting HC is pretreated with ionic detergent solution to mitigate the effect of surface electrostatic charge.[8,9,19] However, in our study we found that the FPM improvement associated with wash-rinse pretreatment was statistically significant only with the OptiChamber Advantage (2-s delay data), and the corresponding FPM values slightly decreased with the PocketChamber (see Tables 2 and 3). The lack of a consistent and statistically significant improvement in FPM with prewashed nonconducting devices (compared to no prewash) is most likely attributable to the low FPM values associated with delayed sampling, in relation to the magnitude of the associated inter-device variability. For example, the FPM values with the BreatheRite, PocketChamber, and ACE were < 7 μg/actuation, even with the 2-s delay. This lack of improvement in emitted FPM with prewashing was worse with the 5-s delay, with which FPM values were correspondingly reduced, because the longer delay increased gravitational settling in the HC. In contrast, the 2 nonelectrostatic HCs (AeroChamber Max and Vortex) were each more than twice as efficient as the best-performing nonconducting HC at optimum use (prewashed with 2-s delay [see Table 3]). From our findings it also appears that the wash/rinse pretreatment may be less influential on FPM than is the use of conducting materials for HC construction.

FPM from the AeroChamber Max (21.5 ± 3.2 μg/actuation) was significantly greater than from the Vortex (15.5 ± 2.0 μg/actuation) when prewashed and evaluated with the 2-s delay. We theorize that this difference may be because of the vortex airflow pattern in the Vortex device,[26] which might increase particle-loss to the chamber walls because of greater turbulent inertial deposition.[27] Further work would be required to substantiate this explanation. No increase in FPM was found with prewashing with these HCs, as expected, due to charge reduction.

Although there were decreases in emitted drug with the longer (5-s) delay with the nonconducting HCs tested without wash/rinse pretreatment (see Table 2), these differences were small in absolute terms and in some instances were statistically insignificant. We believe that this difference was largely because the FPM values were low with these devices, even after a delay as short as 2 s. With the 2 nonelectrostatic HCs, which had larger FPM values, we also observed that decreases in FPM (as a percentage of mass emitted from the inhaler alone) associated with increasing the delay from 2 s to 5 s were small and generally statistically insignificant.

Our results are similar to those of Wildhaber et al,[10] who reported an insignificant decline in fine-particle delivery of albuterol from the stainless steel (conducting) NebuChamber (AstraZeneca, Sweden) with increasing the delay from 1 s to 5 s.

Our data showing large differences in FPM and TEM between nonelectrostatic and nonconducting HCs might be expected to affect clinical outcomes, particularly with bronchodilators, the dose-response relationship of which has been widely studied. However, Dompeling et al[28] found no significant difference in bronchodilation (as measured by peak expiratory flow) in children given HFA-albuterol via 2 nonconducting HCs prewashed with ionic detergent, compared with the stainless steel (conducting) NebuChamber. Taken at face value, that study implies that prewashing a nonconducting HC may be as effective as using a conducting HC in minimizing electrostatic loss of drug particles, and the study therefore appears to contradict the findings of the present study. In explanation, it is possible that differences in emitted HFA-albuterol with prewashing versus use of a nonelectrostatic chamber may not make a clinical difference.

However, Dompeling et al acknowledged 2 limitations that may have accounted for the lack of a difference in their study.[28] First, the children tested had excellent inhaler technique, beginning inhalation immediately after pMDI actuation, with little or no delay, and, second, their measured peak expiratory flows, taken as the indicator of bronchodilation, may have already plateaued at the high end of the dose-response curve. Furthermore, they did not rinse their HCs after washing, in contrast with the practice in the United States, where rinsing is advocated, to avoid patient-contact of detergent-coated surfaces. In this context, it is relevant that Piérart et al[19] observed that water-rinsed, drip-dried nonconducting HCs retained substantial residual electrostatic charge, which was associated with reduced aerosol delivery. However, as they did not investigate the effect (if any) of water rinsing after washing in detergent solution, it is uncertain whether the residual

charge would have been more effectively removed had they followed this procedure that we adopted in our study.

It is recognized that impactor measurements based on sampling the aerosol at a constant flow rate do not simulate the continuously variable flow profile associated with an actual respiratory cycle.[24] Clinical evaluation is therefore needed to determine if our observed bronchodilator FPM differences among these HCs translate to measurable clinical differences.

We also acknowledge that in this study we did not investigate HFA-based pMDI drug formulations other than one particular albuterol-based formulation (Ventolin-HFA). There were 2 reasons for this decision. First, reduction of FPM attributable to electrostatic charge effects could be potentially important for a rescue medication such as a short-acting bronchodilator. A primary intent of our study was to quantify the importance of the choice of conducting or nonconducting materials for HC construction with delivery of HFA-albuterol as a representative β_2-agonist bronchodilator. Second, Peart et al[13] have shown that Ventolin-HFA has a substantial net electronegative charge associated with particles < 5 μm aerodynamic diameter, which are in the size range most likely to be emitted from an HC when inhalation takes place.[4]

We further acknowledge that successive actuations of medication into these HCs may have modified their electrostatic charge properties (the so-called priming effect), resulting in improved delivery. However, the evidence from Berg et al,[29] who investigated this effect with both nonelectrostatic and nonconducting HCs, is inconclusive with respect to the magnitude of the effect on medication delivery from the nonconducting devices, although no priming effect was apparent with their nonelectrostatic spacer.

A final limitation of the present study was our choice to exclude conducting HCs that are currently available only outside of the United States, in particular the stainless steel NebuChamber.[9,30] The use of a metallic HC has been proposed to avoid electrostatic charge accumulation,[30,31] but these HCs are opaque, so it is not possible to see the formation or delivery of the aerosol plume, which appears to be desirable because it provides an indication that the medication is being delivered.[23] Furthermore, in justification of our decision not to include the NebuChamber in this study, the NebuChamber has been shown to have similar performance to that of the AeroChamber Max with chlorofluorocarbon-budesonide and a 5-s delay.[32]

Conclusions

This laboratory investigation, which simulated delayed inhalation with HCs, shows significantly greater FPM of HFA-albuterol with HCs made from nonelectrostatic materials than from HCs made from nonconductive materials, even after wash/rinse pretreatment. Of the 2 nonelectrostatic HCs we tested, the AeroChamber Max delivered more HFA-albuterol in the fine-particle size range, irrespective of pretreatment or delay interval. Additional clinical studies are needed to evaluate the importance of these differences with regard to patient outcomes.

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