Evaluation of Delivery Efficiency from Valved Holding Chambers with Facemasks Under Simulated Use Conditions

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INTRODUCTION

Valved holding chambers (VHCs) in conjunction with a facemask are often used by young children who are unable to use pressurized metered dose inhalers (pMDIs) effectively (1-2). Facemasks are often overlooked as a factor which can influence inhalation drug therapy because of the high cost, variable findings, and ethical quandaries regarding using young children as subjects in clinical studies. The lack of a standardized way to connect facemasks to conventional *in vitro* aerosol testing equipment is an additional complication (3). However, recent studies have demonstrated that facemasks play an important role in drug delivery from VHCs (4-5), and soft anatomical model (SAM) face replicas have been used to preserve clinical relevance during *in vitro* testing with facemasks (6). SAM-based *in vitro* test equipment has now evolved to simulate facemask height, applied force and application angle during evaluation of VHCs with facemasks under simulated breathing conditions (7). This paper builds on a previous study (7) to compare the percent facemask seal leakage and drug delivery efficiency from three VHC-facemask systems.

METHODS

SAM Face Replica Leakage Validation

Percent leakage across the face replica and filter was tested as in Figure 1, and defined as:

Percent leakage = ((Q2-Q1)/Q2)*100

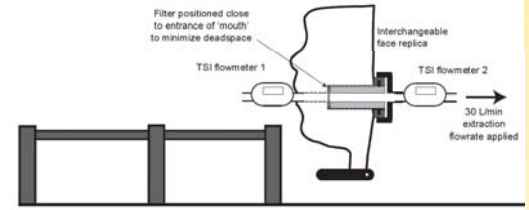

Figure 1. Setup to determine internal face replica and filter leakage.

Leakage across the face replica was determined to be 1.5% at a constant simulated inhaled airflow rate 30 L/min, which was judged to be satisfactory

Facemask Leakage and Albuterol Delivery Efficiency Tests

All VHCs were of similar volume and dimensions, and claimed to exhibit anti-static properties. Each VHC was tested with its marketed facemask of the recommended size:

1. Pre-production OptiChamber Diamond VHCs with LiteTouch facemasks (Philips Respironics, Parsippany, NJ)
2. AeroChamber® Plus Z STAT® VHCs with ComfortSeal® facemasks (Monaghan, Plattsburg, NY)
3. Vortex® VHCs with Spinner® Duck facemasks (PARI, Midlothian, VA)

First, the optimal facemask position on the face for each VHC-facemask system was determined, as shown in Figure 2 (Actuator A). VHC-facemask systems and Actuator A were sealed to prevent leaks unrelated to face seal. A 1.9 kg applied force held the facemask to the face replica while constant flows of 15 and 30 L/min were applied. The height of the face replica in relation to the facemask was adjusted until leakage was minimized for each VHC-facemask system.

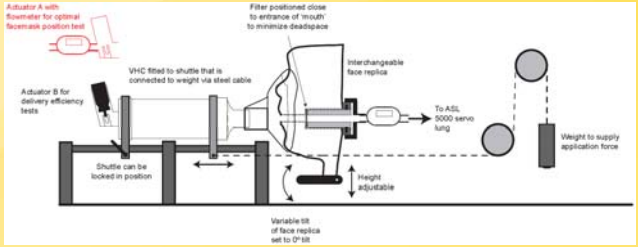

Figure 2. Setup to determine optimal VHC-facemask system position on face replica using the lowest leakage rate approach (Actuator A), and to determine delivery efficiency (Actuator B).

Albuterol delivery efficiency for each VHC-facemask system was determined, as shown in Figure 2 (Actuator B). The downstream side of the face replica/filter was connected to a breathing simulator (ASL 5000, IngMar Medical, Pittsburgh, PA) validated to output a pediatric breathing pattern (tidal volume=155 ml, breathing rate=25 breath/min, inhalation to exhalation ratio=40:60). Each VHC-facemask system was tested with either 0.45 or 1.9 kg applied force under 0° face replica tilt for 1 simulated pediatric breath, example shown in Figure 3.

Five pMDI actuations were actuated into the VHC during each test to ensure a quantifiable amount of albuterol was collected on the filter. Albuterol sulfate recovered from the filter (*Filter Dose*) and VHC/facemask/actuator (*Undelivered Dose*) was quantified by HPLC and used to calculated

Albuterol Delivery Efficiency = (Filter Dose/(Filter+Undelivered Dose))*100

Figure 3. Photos of each VHC-facemask system tested under 0° deg face replica tilt, 1.9 kg applied force for 1 simulated pediatric breath: (Left) OptiChamber Diamond-LiteTouch, (Middle) AeroChamber Z Stat-ComfortSeal, (Right) Vortex-Spinner Duck.

RESULTS AND DISCUSSION

Facemask leakage test results

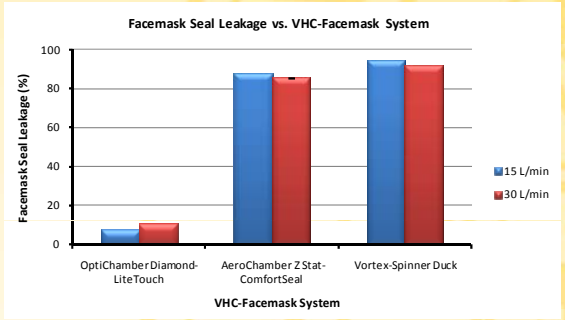

Figure 4. Percent leakage between the facemask and face replica (Bars represent Mean ± SD, n=3).

The LiteTouch facemask exhibited the lowest leakage (approximately 7 and 10% at 15 and 30 L/min, respectively), while the Spinner Duck facemask exhibited the highest leakage (approximately 94 and 91% at 15 and 30 L/min, respectively).

Albuterol delivery efficiency test results

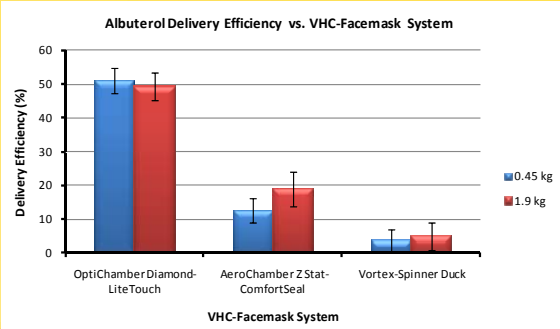

Figure 5. Mean Albuterol Delivery Efficiency for three VHC-facemask systems under either 0.45 or 1.9 kg applied force (Bars represent mean ± SD, n=3).

The delivery efficiency of the OptiChamber Diamond-LiteTouch system was significantly higher than both the AeroChamber Z Stat-ComfortSeal and Vortex-Spinner Duck systems under the same applied force ($p<0.05$). This was attributed to the more efficient face seal in the LiteTouch, which allowed more airflow, and subsequently more complete drug entrainment and emptying from its OptiChamber Diamond VHC and onto the filter during each simulated inhalation.

CONCLUSIONS

- Facemask designs that minimized leaks between the facemask sealing system and the face model increased albuterol delivery efficiency.
- The horizontal test rig facilitated *in vitro* VHC-facemask evaluation in a manner that closely mimics the clinical situation.

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