In vitro Delivery Efficiency of Valved Holding Chambers with or without Facemasks

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Summary

An in vitro method has been described and refined previously for the performance evaluation of valved holding chamber (VHC)-facemask systems. The purpose of this study was to evaluate the delivery efficiency of three commercial VHC-facemask systems: AeroChamber Plus Flow-Vu VHC with ComfortSeal facemask (ACP-FV); OptiChamber Diamond VHC with LiteTouch facemask (OCD-LT); Vortex VHC with Felix Frog facemask (VTX-FR) at simulated pediatric conditions. The study comprised of standardized methods to evaluate VHC-facemask seal leakage against a soft anatomical model (SAM0) and evaluation of delivered dose under an age-specific pediatric breathing pattern which was simulated using an ASL Servo Lung. The results showed that the OCD-LT system formed an effective seal at both application forces (% leakage = 47.4% at 1 lb and 46.5% at 4 lb), whereas the ACP-FV system achieved an effective seal only at high application force (% leakage = 89.8% at 1 lb; 55.6% at 4 lb). The VTX-FR system did not achieve an effective seal in any test condition. Facemask seal leakage reflected delivery efficiency. The ACP-FV system had good delivery efficiency (% delivered dose = 38-43%) at high application force (4 lb) but poor delivery efficiency (% delivered dose = 0.7-1.8%) at low application force (1 lb). The OCD-LT system resulted in the most consistent delivered dose even at low application forces (% delivered dose = 35-42% at 1 lb, 41-47% at 4 lb). When the VHCs were tested without facemask (complete seal) they all produced a good delivery efficiency (% delivered dose; 45-55 for OCD, 41-49% for VTX, and 55-58% for ACP).

Introduction

Valved holding chambers (VHCs) are frequently prescribed with pressurized metered dose inhalers (pMDIs) for patients with poor inhalation technique, such as young children and infants.1) The performance evaluation of VHC-facemask systems involves multiple factors that require a large sample size for a comparative clinical study. An in vitro method using a horizontal test rig has been described and refined previously for the performance evaluation of VHC-facemask systems.2-4) Cost-effective and reproducible, the performance evaluation is carried out under clinically relevant, yet standardized conditions, including age-specific breathing profiles and face models, facemask applied forces, and facemask position and application angles.2-4) The purpose of this study was to evaluate the delivery efficiency of three commercial VHCs with or without facemasks with simulated paediatric conditions.

Materials and Methods

Three antistatic VHC-facemask systems including AeroChamber Plus® Flow-Vu® VHC with ComfortSeal® facemask (ACP-FV, Monaghan Medical Corp., Plattsburg, NY), OptiChamber Diamond® VHC with LiteTouch® facemask (OCD-LT, Philips Respironics, Respirronics New Jersey Inc., Parsippany, NJ), and Vortex® VHC with Felix Frog facemask (VTX-FR, PARI, Midlothian, VA) were selected for this study. A custom-built horizontal test rig and a soft anatomical model (SAM0, representing a four-year old) were used. The facemask seal leakage was assessed under constant flow rate (Q = 15 or 30 L/min) to determine the "best" fit at constant applying forces (delivered by 1 or 4 lb weight). (Figure 1) The “best” fit was defined by the least amount of calculated leakage (eqs. 1a and b) from the facemask seal when the relative positions (height and tilting angle) between SAM0 and VHC-facemask system were adjusted on
Figure 1. Setup to determine “best” VHC-facemask position on face replica (height and tilting angle) and setup to test without facemask (complete seal condition).

the horizontal test rig. The difference in airflow rate ($\Delta$Flow, L/min) was determined by measuring airflow rate upstream of the pMDI inlet and downstream of the filter in the face replica.  

$$\%\text{leakage at 15 L/min} = \frac{\Delta \text{Flow}}{15} \times 100\% \quad \text{(Eq.1a)}$$

$$\%\text{leakage at 30 L/min} = \frac{\Delta \text{Flow}}{30} \times 100\% \quad \text{(Eq.1b)}$$

The “best” fit position, with the lowest seal leakage for each of the three VHC-facemask systems was used for the delivery efficiency evaluation. The age-specific pediatric tidal breathing pattern (tidal volume = 155 mL; inspiration:exhalation = 40:60; breathing rate = 25 breath/min) was simulated and monitored in real time, using a Servo Lung system (ASL 5000 Servo Lung, IngMar Medical, Pittsburgh, PA). An albuterol sulfate suspension pMDI, ProAir HFA (Teva Specialty Pharmaceuticals, Horsham, PA) was used in the test. Delivered dose content uniformity of each pMDI was monitored using dose unit sampling apparatus (DUSA, Copley Scientific, Shoreview, MN) at a constant flow rate of 28.3 L/min. Emitted dose was defined as the dose of albuterol sulfate deposited in the actuator, filter and DUSA. The procedure for pMDI actuation and VHC-facemask systems application at a certain point in the inhalation cycle was described previously.  

The albuterol sulfate deposition in each component was analyzed by high performance liquid chromatography (Hitachi L-7000 series, Spherex 5 $\mu$m C$_18$ 250 x 4.6 mm reverse phase column, Phenomenex, Torrance, CA). The percent delivered dose was determined using eq. 2 at given test conditions including VHCs (ACP-FV, OCD-LT, and VTX-FR), applied forces (1 and 4 lb), and number of breaths (2, 4, and 8 breaths). Each condition was repeated in triplicate ($n = 3$). The %delivered dose was also evaluated without facemask (complete seal condition).

$$\% \text{delivered dose} = \frac{\text{Filter deposition}}{\text{(Filter + VHC + Actuator) deposition}} \quad \text{(Eq. 2)}$$

Results and Discussion

The values of $\Delta$Flow (L/min) and the percent seal leakage (%) obtained at two airflow rates, when the relative heights and tilting angles between VHC-facemask and face replica were at their “best” positions for each applied force, are shown in Table 1. The OCD-LT system formed an effective seal at both application forces (47.4% at 1 lb and 46.5 % at 4 lb), whereas the ACP-FV system only achieved an effective seal at high application force (89.8 % at 1 lb and 55.6 % at 4 lb). The %leakage of the VTX-FR system was 100% at 1 lb force, indicating that no effective seal was achieved at this condition. The result also indicated that the lowest seal leakages for each VHC-facemask system were often but not always achieved when the VHC-facemask systems were positioned horizontally. Distortion of facemasks and SAM0 at different application forces may require adjustment of tilting angles up or down to achieve lowest seal leakage. Delivered dose content uniformity evaluated using DUSA was satisfactory. The percent delivered dose for the three VHC-facemask systems is illustrated in Figure 2.
Table 1. The values of $\Delta$Flow (L/min) and the percent seal leakage (%) obtained at two airflow rates, when the relative heights and tilting angles between VHC-facemask and face replica (SAM0) were at their “best” positions.

<table>
<thead>
<tr>
<th>VHC-facemask</th>
<th>$\Delta$Flow @ 15 L/min</th>
<th>$\Delta$Flow @ 30 L/min</th>
<th>% leakage @ 15 L/min</th>
<th>% leakage @ 30 L/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACP-FV</td>
<td>14.8 ± 0.3</td>
<td>26.9 ± 0.8</td>
<td>98.7 ± 1.8</td>
<td>89.8 ± 2.7</td>
</tr>
<tr>
<td>OCD-LT</td>
<td>6.4 ± 0.4</td>
<td>14.2 ± 0.5</td>
<td>42.8 ± 2.9</td>
<td>47.4 ± 1.6</td>
</tr>
<tr>
<td>VTX-FR</td>
<td>15</td>
<td>30</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

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<th>VHC-facemask</th>
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<th>% leakage @ 15 L/min</th>
<th>% leakage @ 30 L/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACP-FV</td>
<td>9.3 ± 0.8</td>
<td>16.7 ± 1.1</td>
<td>62.1 ± 5.0</td>
<td>55.6 ± 3.8</td>
</tr>
<tr>
<td>OCD-LT</td>
<td>6.4 ± 0.1</td>
<td>13.9 ± 0.1</td>
<td>42.9 ± 0.5</td>
<td>46.5 ± 0.4</td>
</tr>
<tr>
<td>VTX-FR</td>
<td>15</td>
<td>28.4 ± 0.5</td>
<td>100</td>
<td>94.6 ± 1.6</td>
</tr>
</tbody>
</table>

Effect of seal leakage: Facemask seal leakage can profoundly reduce the delivered dose and increase delivered dose variability. In this study, the ACP-FV and VTX-FR systems had very poor facemask seal at low application force (1lb). This resulted in a delivered dose of less than 5%. In contrast an effective seal was evident even at the low level of applied force when testing the OCD-LT system, and delivered doses were in the range of 35-42% depending on the number of breaths. Using the high level of applied force (4 lb) resulted in increased percent delivered doses from the ACP-FV system (38-43%), which were similar to those of the OCD-LT system (41-47%). Even at high application force, the VTX-FR system could not form an effective seal and the delivered dose was less than 5%. When facemasks were removed and a complete seal condition was tested, the ACP-FV system resulted in the best performance.
(55-58%), followed by the OCD-LT system (45-55%), and then the VTX-FR (41-49%) system. This indicates that facemask leakage has the most significant effect on the performance outcome. It also indicates that the Felix Frog facemask for VTX could not achieve a good seal and this is probably the main reason for the poor performance.

**Effect of Number of Breaths:** The number of breaths from 2 to 4 to 8 breaths resulted in a slight increase in performance outcome in both high and low seal leakage conditions.

**Effect of VHC-facemask design:** The OCD-LT system uses soft-seal mask technology that promotes an efficient seal even at low application force (1 lb) and results in good percent delivered dose (35-42%). High application force may contribute to distress of young patients during treatment and is therefore best avoided. The double-flange inward-curled design used in the ACP-FV and OCD-LT system facemasks are better-adapted to the nasal bridge and force-responsive 3D contour of the face and gave better facemask to SAM seal than the VTX-FR system facemask. Both the ACP-FV and OCD-LT systems have a flow indicator on the VHCs that help breath counting and allow monitoring of the breath holding maneuver. The OCD-LT system has a high-flow whistle that gives an alarm when the inspiratory flow rate is too high. These features may improve inhalation technique and further increase delivery efficiency.

**Conclusion**
The horizontal test rig provides a useful tool to conduct in vitro performance evaluation and assess variability in delivered dose from different VHC-facemask systems. In this study, the performance efficiency of three commercial VHC-facemask systems was evaluated. The result showed that the OCD-LT system had the lowest leakage at low application force and the VTX-FR system had the highest leakage even at high application force. In many cases, the lowest seal leakage was achieved at 0° tilting angle. The OCD-LT system resulted in the most consistent delivered dose at different application forces. The ACP-FV system had good delivery efficiency at high application force and under the completely sealed condition. The VTX-FR system resulted in good delivery efficiency only in complete sealed condition. Increasing the number of breaths resulted in a trend to a slight increase in performance. The in vitro performance test provides a valuable VHC-facemask screening tool that allows focus on optimizing key components of the VHC-facemask systems.

**Reference**