Addressing the patient-device use interface: Development and laboratory validation of a facemask with anatomically-responsive face models

Face models facilitate critical performance evaluation of orally inhaled products in clinically-appropriate ways

Jolyon P. Mitchell, Robert W. Morton, Dan Engelbreth, Mark W. Nagel and Dominic P. Coppolo

Trudell Medical International* and *Monaghan Medical Corporation

Many patients, particularly the very young, the elderly and those with co-morbidities affecting coordination, need to use a facemask rather than a mouthpiece in order to receive inhaled medication via a pressurized metered dose inhaler with valved holding chamber (pMDI-VHC). The VHC is therefore an integral component of the drug delivery system, necessitating that a meticulous and thorough approach be taken to optimize all aspects of its performance. This article explores the steps taken to design a range of facemasks that are age-of-user-appropriate. In addition, it discusses the ways the infant version has been validated in the laboratory using an anatomically-appropriate face model, in which the surfaces coming into contact with the facemask have similar responsiveness to human soft facial tissues.

Introduction

The interface for a pMDI-VHC for use by non-mechanically ventilated patients can either be a mouthpiece or facemask.[1] The former is more appropriate for older children and adults who can coordinate inhaler actuation with the onset of inhalation,[2] or who are capable of achieving a maneuver that involves a slow deep inhalation followed by a breath hold.[2] However, infants and younger children are seldom able to achieve this degree of skill and a facemask is therefore the preferred interface for these users.[3] The use of VHCs with attached facemask is therefore in widespread use for younger pediatric patients with obstructive lung disease. Similarly, a facemask may be more appropriate for use by the elderly, especially those with co-morbidities affecting motor skills.[4] At least one study with elderly patients receiving bronchodilators has concluded that the use of a facemask, together with improved technique available with a pMDI-VHC combination, provides clinical equivalency to nebulization.[5]

Attributes of a well-designed facemask

The International Society for Aerosols in Medicine (ISAM) Focus Symposium on the topic: "The Interface Between the Device and the Patient: Masks, Mouthpieces and 'Others,'" held in the spring of 2005, was an opportunity for experts involved with the design, development and evaluation of inhalers to agree about the factors that need to be present in a well-designed facemask for a VHC.[6] The following attributes were considered important:

1. The facemask must seal properly to the face to avoid ingress of ambient air via leakage pathways that can greatly dilute the aerosol available to be inhaled;

2. The volume of the dead-space defined by the contours of the face and inner surface of the facemask should be minimized to avoid loss of aerosol during exhalation in cases such as with infants, in which more than one breathing cycle is needed to empty the contents of the VHC;

3. Soft facemasks with in-built flexibility do a better job of minimizing this dead-space when applied

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with a clinically-appropriate force than facemasks manufactured from rigid polymer;

4. Facemasks that have contoured rolled edges that are flexible are more comfortable for patients than those having sharp or rigid edges and are therefore more likely to be tolerated by infants and small children;

5. Facemasks intended for use by infants or small children should reflect the different facial contours for these sub-groups and not be merely scaled-down versions of adult facemasks;

6. The facemask should contain a low resistance valve that opens upon exhalation and is closed during inhalation to improve patient comfort and, more importantly, avoid the need to remove the facemask during each exhalation; the exhalation valve should be positioned such that the exhalation flow is directed away from the VHC.

The use of anti-static materials in facemasks was not considered important (although surface electrostatic charges may be present when removed from the packaging). This is likely because the act of exhalation into the facemask, which often occurs before the first inhalation, creates a near-to-saturated environment in the dead-space that effectively dissipates charge.

Evolution of the ComfortSeal facemask

The development of the ComfortSeal facemask (Trudell Medical International, London, Canada) provides a good illustration of the ways attention was paid to each of the attributes just described. The latest version of this facemask is used in conjunction with the currently available antistatic AeroChamber Plus Flow-Vu family of VHCs.

The original AeroChamber VHC, which was developed in the early 1980s, was supplied only with a mouthpiece. Soon after the product was launched, however, the need for a facemask interface was recognized. In 1988, a family of VHC-facemask products was provided for infants, children and adults (referred to as small, medium and large masks, respectively, in the United States). Even at this early stage of development, it was recognized that a patient age-specific approach was needed for facemask design so that the dead-space inside the facemask, when fitted, could be minimized. Each silicone facemask had a sharp-lipped conical profile in cross-section and was therefore sized appropriately for the intended user age group. Figure 1 represents a sideview of an early AeroChamber VHC with medium facemask.

At the outset, it was recognized that both the mouth and nose needed to be enclosed by the facemask to ensure medication delivery was possible by either route of administration. This requirement is self-evident for infants younger than 9 months of age who preferentially breathe through the nose,[7,8] but it is also important for older users who often inhale both through the nose and orally.[8] In addition, it was essential for the caregiver to achieve a facemask-to-face seal easily when treating infants or small children so the material of construction for the facemask was flexible silicone rubber.

By the early 1990s, the importance of minimizing the dead-space between the inhalation valve of the VHC and the nose/mouth of the patient was becoming apparent.[9] The chosen solution was locating the exhalation valve in the facemask, since this arrangement was compact and permitted exhalation with the mask remaining in position on the patient's face. Flow from the exhalation valve was directed away from the eyes to avoid exposure to medication that might, in some instances, exacerbate narrow-angle glaucoma.[10] The second generation facemask, introduced in 1992, remained conical (Figure 2). A rudimentary means of verifying the effectiveness of the seal to the face was provided

Figure 1

First generation cone-shaped facemask supplied with AeroChamber VHCs

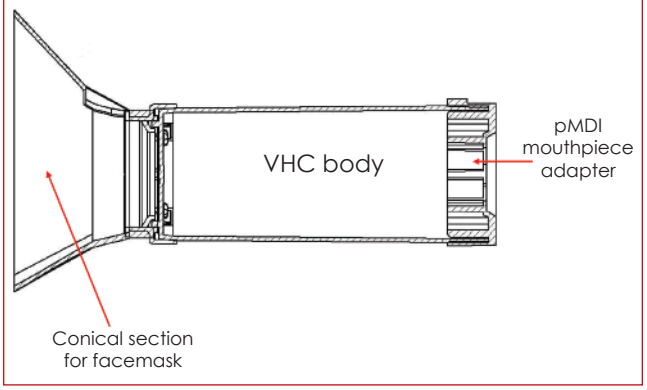
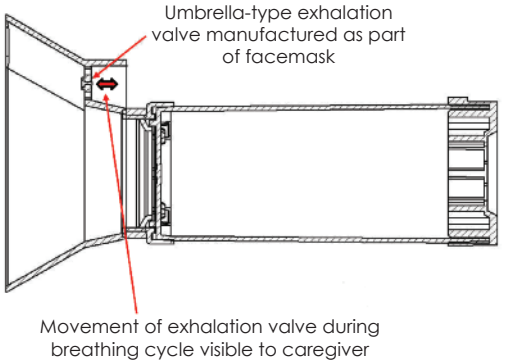


Figure 2

Second generation conical facemask supplied with AeroChamber VHC



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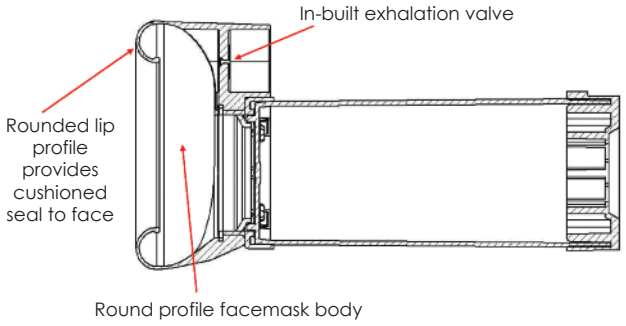
by a caregiver observing the movement of the umbrella-type exhalation valve in response to the respiration of the patient receiving treatment.

The next stage in the evolution of the facemask came about in the mid-1990s, when it was evident that compliance, particularly with infants and small children, could be improved if the feel of the facemask was made more comfortable when applied firmly to create the necessary seal. This consideration is significant, since the most common cause of failing to achieve an effective seal had been identified as distress engendered in infants and toddlers.[11]

The rounded lip, flexible, silicone facemask (Figure 3), introducing the name ComfortSeal for the first time, was launched in 1996, also retaining the exhalation valve in the facemask.

Figure 3

First generation ComfortSeal facemask supplied with AeroChamber VHCs



The development of the AeroChamber Plus VHC family took place in the late 1990s, to provide more efficient aerosol delivery and, at the same time, to respond to changes in pMDI aerosol plume behavior associated with the replacement of chlorofluorocarbon by hydrofluoroalkane propellants in pMDI formulations.[12] Concurrently, internal research at Trudell Medical International, into the age-related development of anthropomorphic facial shapes and dimensions critical for facemask sealing to faces of infants/children, indicated that the facemask design could be improved still further to ensure a better seal to the facial contours. Such improvement is particularly desirable with infants and small children, where correct positioning of the VHC-facemask can be difficult to attain if the child is uncooperative.[13] Between December 1998 and February 1999, additional data were obtained for facial sizes, including different ethnic groups.[14-16]

Several critical parameters were identified to guide the re-design of the infant and child facemasks:

a. The boundary between age ranges for "infant" and "child" facemasks was defined as age 18 months;

b. The range for the "infant" facemask was defined as encompassing the majority of users from birth to the upper age limit for this product;

c. The upper boundary of the age range for "child" was defined as 6 years;

d. The NIST-derived anthropometric data of 1977[14] were used to define the basic dimensions of each facemask; Figure 4 illustrates the key dimensions and their relationship to the "child" facemask;

e. Shapes of both facemasks were chosen to optimize the creation of a reliable seal onto a contoured facial surface, based on measurements made using appropriate resuscitation mannequins having rigid surface facial features;

f. Leakage at the bridge of the nose (around the eyes) was recognized as being the most likely consequence of an imperfect facemask-to-face seal and was therefore to be addressed as a priority;

g. The dead-space was to be minimized when the facemask was applied to the face with a clinically-appropriate force; this value was eventually set at 1.6 kg, based on concurrent experiments undertaken by clinicians at Wake Forest University School of Medicine, which were later published.[17]

At this stage, the focus of the re-design was on the two pediatric facemasks rather than the adult version. The larger tidal volumes associated with adult patients (typically between 600 and 1,000 mL) meant that dead-space control and facemask-to-face sealing were likely to be less important in terms of guaranteeing reliable aerosol delivery for this class of users.

Prototype facemasks for the new design were subsequently evaluated clinically in a patient-use study undertaken by clinicians at Arkansas Children's Hospital with both male and female infants and children, aged 11 months to 9-years-and-1-month. Apart from collecting demographic information (age, sex and weight), measurements were obtained concerning two critical dimensions relating to facemask fit, namely the height from the bridge of the nose to the chin (A-A' in Figure 4), the width from the left to right cheek (B-B' in Figure 4) and the distance between the midpoint of the nose and midpoint of the partially opened mouth, assuming the gap between lips to be 20 mm along the central axis (C-C' in Figure 4).

The commercialized facemasks transitioned from a circular to a pear-shaped cross-section, comprising a pocket to accept the nose (Figure 4). The curved lip design was retained, providing a cushion-like seal to the face. The exhalation valve was located in the upper part of the facemask. A protective cover

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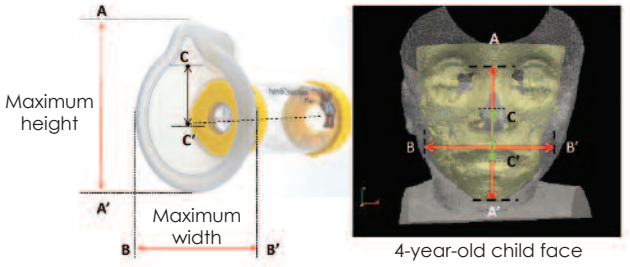
Figure 4

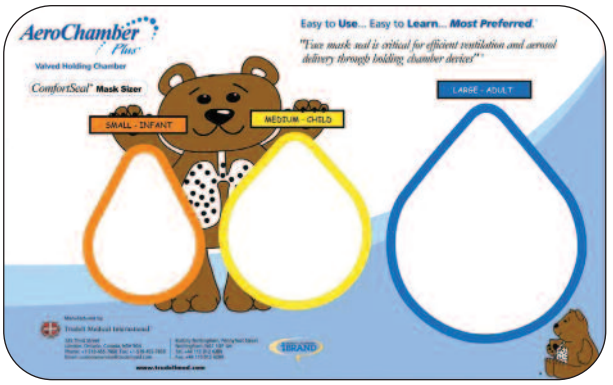
Relationship between Critical Child ComfortSeal facemask dimensions and a reconstructed facial image for a 4-year-old child; the separations between midpoint of the nose and mouth were determined with the mouth closed and also opened to a lip-separation of 20 mm



was also provided externally for the valve to prevent damage caused by tampering, likely with small children. By the mid-2000s, the adult facemask was also updated to include these design improvements. Each facemask has a different internal design to optimize fit to the appropriate age group of patients.[18] A facemask sizing gauge (Figure 5) was developed, containing cut-outs representing the facemask outlines, as an aid to clinicians to fit a patient to a specific facemask size. This approach has since been widely adopted by suppliers of VHC-facemask products.

Figure 5

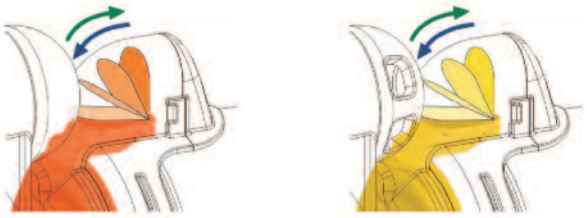
Facemask sizing aid showing infant, child and adult fit profiles; the mouth and nose of the patient are fitted through the appropriate profile



The addition of an inspiratory flow indicator (Flow-Vu IFI) to the AeroChamber Plus VHC family in 2008 was the next significant improvement to the design of the device, as it provided positive feedback to the clinician and caregiver concerning effectiveness of medication delivery. The forward and backward motion of the inspiratory flow indicator is directly linked to the opening and closing of the inhalation valve in response to the respiration of the user (Figure 6). In addition, its movement confirms to the caregiver that the facemask is properly sealed to the patient's face. Under these circumstances, the flow generated when the patient inhales operates the inhalation valve of the VHC, rather than drawing in air from location(s) where the mask-to-face seal is inadequate and diluting the inhaled aerosol.

Figure 6

Flow-Vu Inspiratory Flow Indicator (IFI) shown with (a) infant and (b) child VHCs



If the seal is inadequate, the user may be unable to develop sufficient flow to operate the inspiratory valve. Extensive laboratory testing with a series of face models (Aerosol Delivery to Anatomical Model [ADAM]) subsequently confirmed that a reliable mask-to-face seal could be achieved with the 1.6 kg applied weight as the target clinically-appropriate value.[19-21]

Figure 7 illustrates the current facemasks for the infant, child and adult antistatic AeroChamber Plus VHC products with Flow-Vu indicator, comparing the individual profiles for each facemask size.

Figure 7

(a) Infant, (b) child and (c) adult antistatic AeroChamber Plus VHCs, each with Flow-Vu IFI

Validation of the infant ComfortSeal Facemask in the laboratory

From 2002 onwards, a series of infant,[19] and later small child,[20] face models was developed with the intention of making the response of the modeled facial soft tissues anatomically appropriate. The third-generation Aerosol Delivery to Anatomical Model (ADAM) infant face and upper airway was reconstructed from an MRI scan using 3D-stereolithography. This model has the naso-pharyngeal

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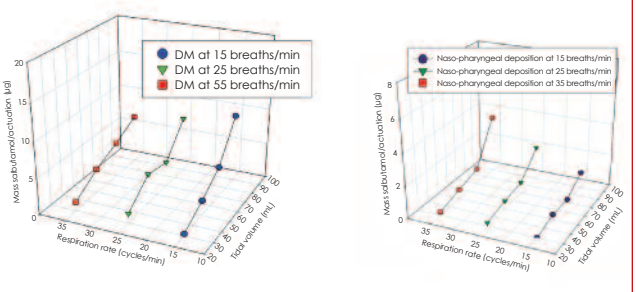
geometry of a 7-month infant[22] and possesses near-to-optimum mechanical responsiveness of the skin and underlying soft tissues when a facemask is applied.[22] In use, the airway of the model is coated with a thin layer of polyoxyethylene lauryl ether surfactant (Brij-35) to simulate the mucosa.[22] Values of delivered mass (DM) of pMDI-delivered salbutamol by infant AeroChamber Plus VHC with Flow-Vu indicator (mean ± SD) to the lungs (4.2 ± 2.0% label claim mass/actuation) were obtained at the model exit for a standard condition of 50 mL tidal volume; 25 breathing cycles/min and 25% duty cycle (inspiratory/expiratory time). They were consistent with clinical data (1.97 ± 1.4%) reported by Tal, et al.[23] with patients having cystic fibrosis, given the likely effect of airway obstruction on medication delivery efficiency. This laboratory investigation[21] also explored the effect of varying tidal volume (30 to 90 mL) and respiration rate (15 to 35 breaths/min). Although most trends were small, delivered drug mass at the distal end of the upper airway, representing delivered mass to the lungs, tended to increase with tidal volume, reflecting more efficient aerosol transport (Figure 8). Drug deposition to the face/nares and also within the airway of the model also increased. Interestingly, although breathing rate increases had a smaller effect on delivered mass, retention of drug in the airway increased significantly at the two highest tidal volumes (70 and 90 mL), indicative of the onset of enhanced inertial deposition at the relatively larger instantaneous flow rates associated with these high respiration rates.

Figure 8

Validation of ADAM-III Infant Model; (a) Delivered mass to lungs (DM); (b): Naso-pharyngeal deposition at various tidal breathing conditions (25% duty cycle)



(a) (b)

Future directions

A child ADAM-III model has also recently been developed by a stereo-lithographic technique similar to that used to produce the infant model. However, the imaging data came from an MRI scan of a 4-year-old male subject having both oral and naso-pharyngeal airways open. The realization of the facial profile, together with the underlying bone structure, has been executed in rigid polymer resin by a similar procedure to that used for the infant model. Validation is being undertaken again using pMDI-delivered salbutamol, but delivered by AeroChamber Plus VHC with Flow-Vu indicator and child facemask.

An adult ADAM-III model is also currently being developed using similar methods as those applied to the child model. Ultimately, it is intended that the suite of ADAM-III faces with upper airways will provide a comprehensive set of models to enable developments of facemasks associated with nebulizers as well as with VHC-based products. These developments recognize the overriding need to evaluate the performance of orally inhaled products with facemasks in clinically-appropriate ways.[24]

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Jolyon P. Mitchell is Scientific Director, Robert W. Morton is Director, New Product Mechanical Development (NPMD) Department, Dan Engelbreth is Industrial Designer, NPMD Department and Mark W. Nagel is Manager, Medical Aerosol Laboratory at Trudell Medical International. Dominic P. Coppolo is Vice President at Monaghan Medical Corporation. Corresponding author: Jolyon P. Mitchell, Trudell Medical International, 725 Third Street, London, Ontario, N5V5G4, Canada, Tel: +1 519 455-7060, JMitchell@trudellmed.com. Website: www.trudellmed.com