Aerosol delivery using pediatric valved holding chamber face masks under real-life application pressure

Yvonne Burmeister[1], Karin Steinführer[2], Luisa Roßmann[3], Arshan Perera[4], Andrea Winzen[3]

[1]PARI GmbH, Starnberg, Germany; [2]PARI Pharma GmbH, Gräfelfing, Germany, [3]PARI*tec* GmbH, Gräfelfing, Germany, [4]PARI Medical Holding GmbH, Starnberg, Germany; Contact: andrea.winzen@pari.com

Background and Objectives

Effective drug delivery via valved holding chambers (VHCs) in pediatric patients critically depends on the integrity of the face mask seal.[1] While regulatory standards recommend an application force of 16 Newtons [N] for in vitro testing[2], real-world data shows that parents typically apply no more than ~4N when treating their 1–4 years old children.[3] At such low forces, insufficient mask sealing can cause substantial leakage and reduced lung deposition.[4] This study evaluated how face mask leakage at a 4N application force influences budesonide delivery, comparing leakage and aerosol performance of five commercially available VHC mask-chamber combinations for babies and young children.

Material and Methods

Using 3D scans of pediatric faces, two anatomical Louis Infant Anatomical Face Models (LIAM) were developed to assess commercially available VHC baby and child masks. These models (Figure 1) accurately replicate the facial geometry and varying firmness of soft tissues and bone structures in children.

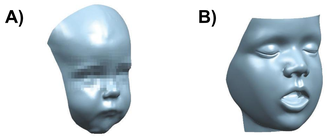

Figure 1: LIAM face model family: **(A)** LIAM Baby (9 months); **(B)** LIAM Infant (2–3 years)

The experimental set-up utilized a modified VHC Shake and Fire Test Stand to assess face mask leakage and respirable doses of budesonide (Figure 2), using the LIAM Baby (9 months) and LIAM Infant (2-3 years) face models. A mask application force of 4N (equivalent to a 408 g weight) was applied via a high-precision force sensor. Mask-to-face leakage [%] was calculated using flow rates upstream of the VHCs and downstream of the face models, according to the following equation: $leakage$ [%] = $(FR_{down} - FR_{up}) / FR_{ref} \times 100$ where FR_{ref} is a constant reference air flow of 30 ± 0.5 L/min used to normalize leakage rates. All aerosol tests were performed using ten doses of budesonide (Budiair®, Chiesi, 200 µg per actuation). Emitted mass (EM) [µg] was measured in accordance with USP <1602> at 4N application force. Breath simulation experiments (BSE) were performed with age-appropriate breathing patterns (baby: TV = 75ml f = 30/min, 1:1 In:Ex; child: TV = 155ml, f = 25/min, 1:2 In:Ex).[4] Additionally, next generation impactor (NGI) measurements were performed at 4N. Aerosol parameters determined at a constant flow rate (30 L/min) included: delivered dose [µg] defined as throat + stage deposition 1-7 + micro-orifice collector, fine particle dose (< 5 µm) [µg], fine particle fraction (FPF) [% < 5 µm] and mass median aerodynamic diameter [µm]. Three devices were tested in triplicates (n = 9). The respirable dose (RD) [µg] was calculated as: *RD = EM x FPF*. This value represents the amount of active ingredient contained in droplets smaller than 5 µm. Detailed test methods for both BSE and NGI are provided in references 5 and 6.

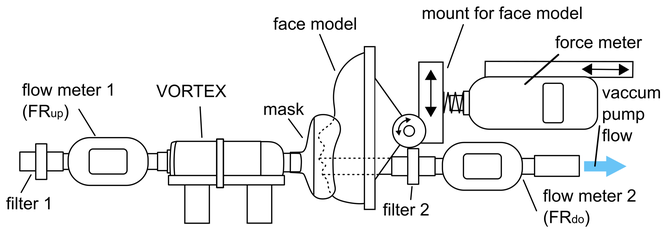

Figure 2: *Schematic sketch of the modified VHC Shake and Fire Test Stand to assess face mask leakage.*

Results

At 4 N application pressure, leakage varied substantially among the tested VHC baby masks. VORTEX® (PARI) and L'Espace® (Air Liquide) exhibited relatively low leakage, with VORTEX achieving the most effective seal. OptiChamber® Diamond (Philips Respironics) exhibited moderate leakage. RC-Chamber® (CEGLA) and AeroChamber® Plus Flow-Vu (Trudell) baby masks showed much higher leakage (Figure 3).

VORTEX's minimal leakage corresponded to the highest respirable dose. Although L'Espace provided adequate sealing, it did not result in a high respirable dose. OptiChamber, RC-Chamber, and AeroChamber Plus Flow-Vu were associated with higher leakage levels and consequently lower respirable doses (Figure 3).

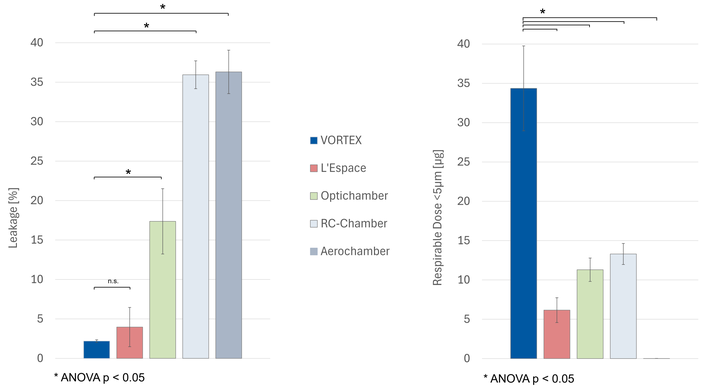

Figure 3: *Leakage and corresponding respirable dose of valved holding chamber baby masks at 4N. Data are presented as mean ± SD. Statistical analysis was performed using one-way ANOVA with a significance level of α = 0.05. Statistical comparisons were made against the chamber exhibiting the lowest leakage rate or the highest respirable dose.*

Among VHC child masks, VORTEX and RC-Chamber demonstrated the lowest leakage rates. OptiChamber Diamond, AeroChamber Plus Flow-Vu and L'Espace showed higher leakage, with L'Espace exhibiting the highest leakage rate, which corresponded to the lowest respirable budesonide dose. Despite moderate leakage, OptiChamber and AeroChamber achieved adequate respirable doses, whereas the superior sealing of VORTEX and RC-Chamber translated directly into higher respirable doses (Figure 4).

While leakage has been confirmed as a critical factor affecting the respirable dose, the results also highlight the influence of additional parameters on the performance of a VHC-mask system. Supporting data can be found in reference 5. Future work will examine these factors further (e.g. valve resistance) and their interaction with overall system performance.

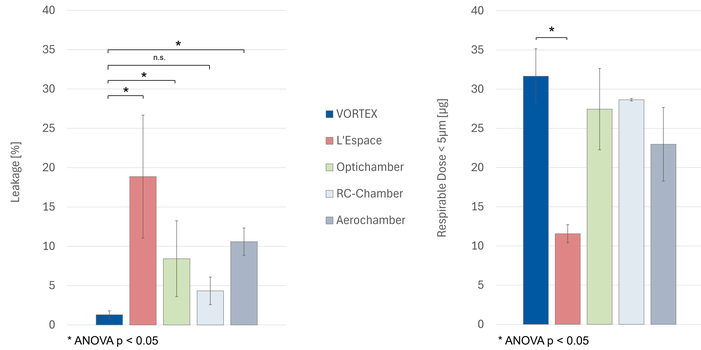

Figure 4: *Leakage and corresponding respirable dose of valved holding chamber child masks at 4N. Data are presented as mean ± SD. Statistical analysis was performed using one-way ANOVA with a significance level of α = 0.05. Statistical comparisons were made against the chamber exhibiting the lowest leakage rate or the highest respirable dose.*

Conclusions

Significant variations in facemask leakage and respirable dose were observed between VHC masks at a clinically relevant application pressure of 4N, underscoring the importance of face mask selection in pediatric therapy. Among all tested VHC masks used with their respective chambers, VORTEX® exhibited the lowest leakage and delivered a high respirable dose, making it the most effective option for babies and children.

References

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