In-vitro Aerosol Deposition of Valved Holding Chambers for Children with Budesonide pMDI

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Aims

- Breathing frequency, tidal volume and inhaler coordination frequently impede efficient pulmonary aerosol delivery by pressurized metered dose inhalers (pMDI) in children [1].
- These constraints can be overcome by using valved holding chambers (VHC) to improve lung deposition.
- Yet, performance and efficiency of today's VHCs is affected by their design and material properties [2].
- This in-vitro study evaluates the aerosol performance of a budesonide MDI combined with four commercially available pediatric VHCs mimicking a child breathing pattern and delayed inhalations (0, 2 and 5 sec).

Material and Methods

New VORTEX®, *PARI GmbH,* **VC**
frog facemask, age 2–4y,

OptiChamber Diamond, *Philips Respironics,* **OC**
age 1–5y,

AeroChamber Plus® Flow-Vu; *Trudell* , **AC**
age 1–5y

L'espace, *Air Liquide*, **LS**
age 2–6y

Figure 1: Tested VHCs with corresponding face masks

- In-vitro tests were conducted with the realistic 3–4 year old child face model LIAM (Louis Infant Anatomical face Model). Each VHC incl. mask was applied with a sufficient force to ensure an adequate seal.
- Standard pediatric breathing pattern (TV = 155 mL, 25/min, 1:2 In:Ex) was performed with a breath simulator PARI Compas II with inhalation delay times of 0, 2 and 5 sec.

Figure 2: Breath simulation experiment with face model LIAM, VHC with facemask and automated MDI shake and fire system for synchronized time delay simulation.

- The VHC/pMDI (Budesonide 200 µg/actuation, Budiair, Chiesi) combinations were mounted in a purpose built shake and fire system capable of simulating arbitrary inhalation delay times by synchronizing the MDI actuation to the breathing pattern.
- The following parameters were determined as a function of inhalation delay and breathing pattern: Delivered dose, DD [%], respirable fraction RF [%<5 µm] determined by a Next Generation Impactor at 0 sec delay at constant flow (30 L/min) and respirable dose, RD = DD x RF. The latter two quantities were determined according to the method described in [3].
- All measurements were done in triplicates. Budesonide was quantified via an internally validated HPLC methodology. Statistics were calculated from 9 individual samples per time delay.

Results

- DD and RD for VORTEX®, AeroChamber Plus® and OptiChamber Diamond decrease with increasing inhalation delay, while DD and RD for L'espace are nearly constant, but at a far lower level.
- Statistical analysis across all time delays (multifactorial ANOVA) reveals significant differences in DD and RD between VHC brands (p<0.05), with VORTEX® reaching the highest values.

Table 1: Summary of DD, RD and MMAD for the investigated VHCs at delayed inhalation and child breathing pattern. Mean (SD) values.

VHC	DD [%] 1)			RD [%] 1)			MMAD [µm]
	0 sec	2 sec	5 sec	0 sec	2 sec	5 sec	0 sec
VC	14.5(1.1)	13.6(1.2)	11.5(1.4)	12.0(0.9)	11.2(1.0)	9.5(1.2)	2.6(0.1)
AC	12.3(2.2)	11.3(2.8)	10.6(1.3)	10.6(1.9)	9.8(2.4)	9.2(1.1)	2.5(0.1)
OC	11.7(0.9)	10.2(1.1)	9.7(0.3)	10.0(0.8)	8.8(1.0)	8.3(0.3)	2.3(0.1)
LS	2.9(0.8)	2.4(0.3)	2.8(2.0)	2.6(0.7)	2.2(0.3)	2.6(1.9)	2.1(0.3)

1) of label claim, 200 µg

- Considering individual time delays (t-test) the VORTEX® yields larger DD and RD than AeroChamber Plus® at 0 and 2 sec delay (p<0.05) and significantly larger DD and RD (p<0.05) than OptiChamber Diamond and L'espace at all time delays (except OptiChamber at 5 sec).
- There are no significant differences between AeroChamber Plus® and OptiChamber Diamond for DD and RD at any given time delay.
- DD and RD for L'espace is significantly lower (p<0.05) at all time delays compared to all other VHCs, but provides the smallest (p<0.001) mass median aerodynamic diameter, MMAD (see Tab. 1).
- Compared to the MDI, oropharyngeal drug deposition is significantly reduced (p<0.001) to less than 1% for all VHCs and time delays (data not shown).

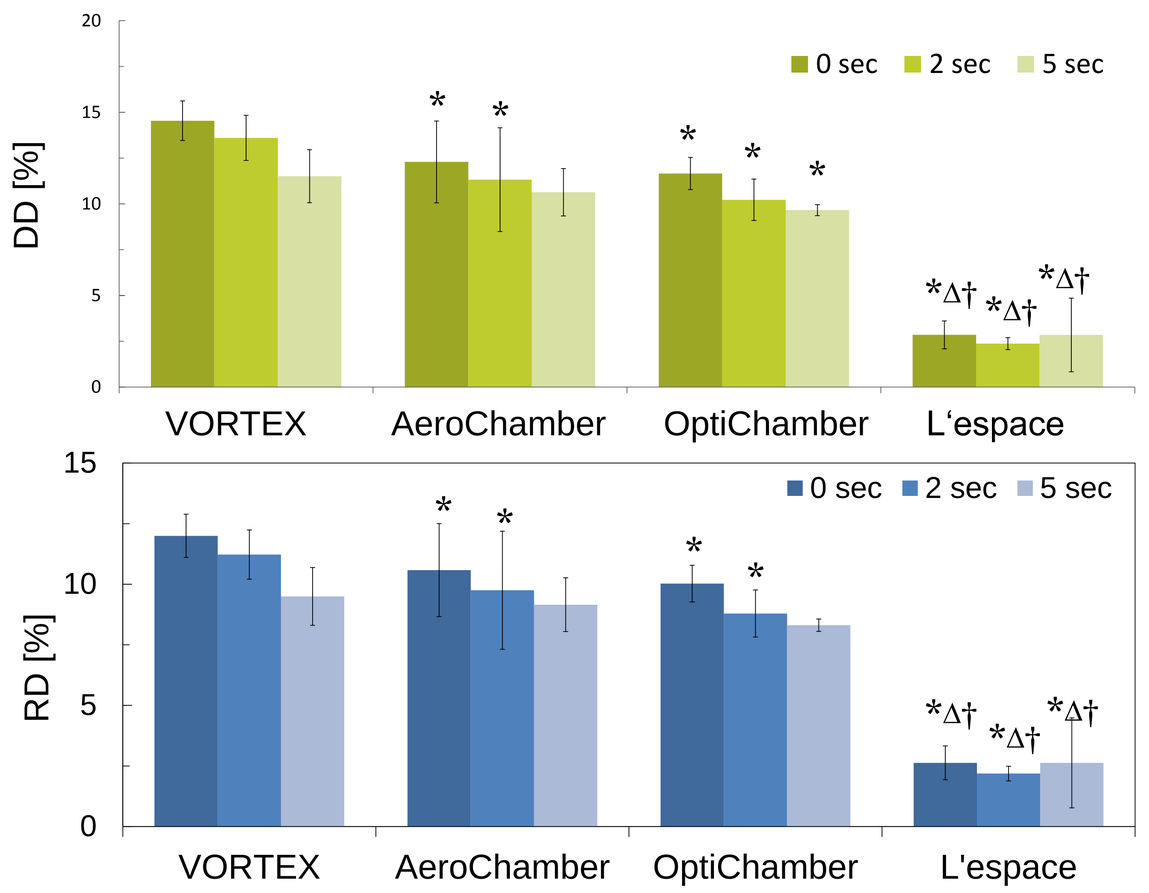

Figure 3: VHC performance as function of inhalation delay and child breathing pattern (TV = 155 mL, 25/min, 1:2 In:Ex): **(top)** Delivered dose, DD; **(bottom)** Respirable dose (<5 µm), RD. (*) denotes significant differences to VORTEX® (p<0.05); (Δ) denotes sig. diff. to AeroChamber Plus® and (†) denotes sig. diff. to OptiChamber Diamond.

Conclusions

- Quantitative data of delivered and respirable dose of a budesonide pMDI administered with four commercially available pediatric VHCs at increasing inhalation delays with a child breathing pattern show significant differences.
- Standardized methodology mimicking real life conditions with minimized failure probabilities by operators is key for realistic VHC comparisons.
- Physicians should be aware that different valved holding chambers for children yield different delivery efficiency. This should be considered in daily practice when choosing an appropriate VHC for children.

References

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