Analysis of the Impact of Specially Designed Annubar Probe (DigitHal®) Flow Meter Inserted into a Valved Holding Chamber

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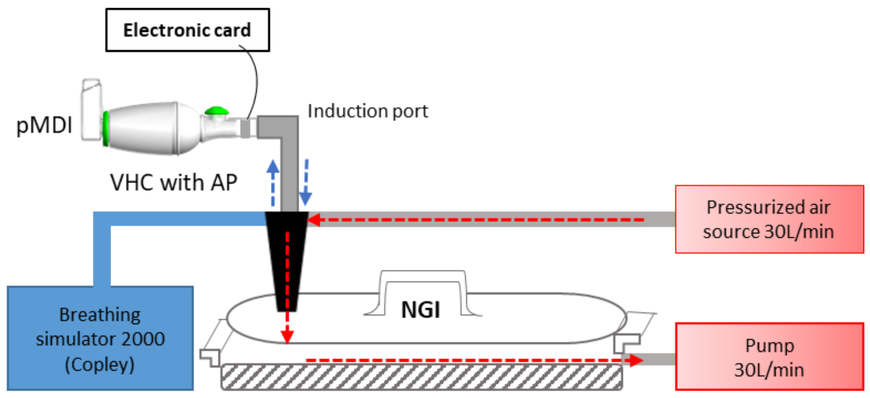
Introduction

To improve inhaled drug delivery, valved holding chambers (VHC) are often used, especially to flow down aerosolized drug from pressurized metered dose inhalers (pMDI). Unfortunately, despite the use of VHC, many patients fail to properly use their devices, leading to exacerbations, limited quality of life [1] and reduced patient adherence [2]. By inserting a Probe (DigitHal®) into the mouthpiece of a VHC, data on the expiratory and inspiratory flow can be collected. This information could be used, by patients and/or caregivers, to help performing a slow and deep inspiration as a recommended when using a VHC [3]. Using *In Vitro-In Vivo* Correlations of inhaled drug (IVIVCs), the capability of the DigitHal® probe to properly analyze respiratory flow was investigated. In the mean time, the potential impact of inserting the probe into the mouthpiece has been investigated.

Material and method

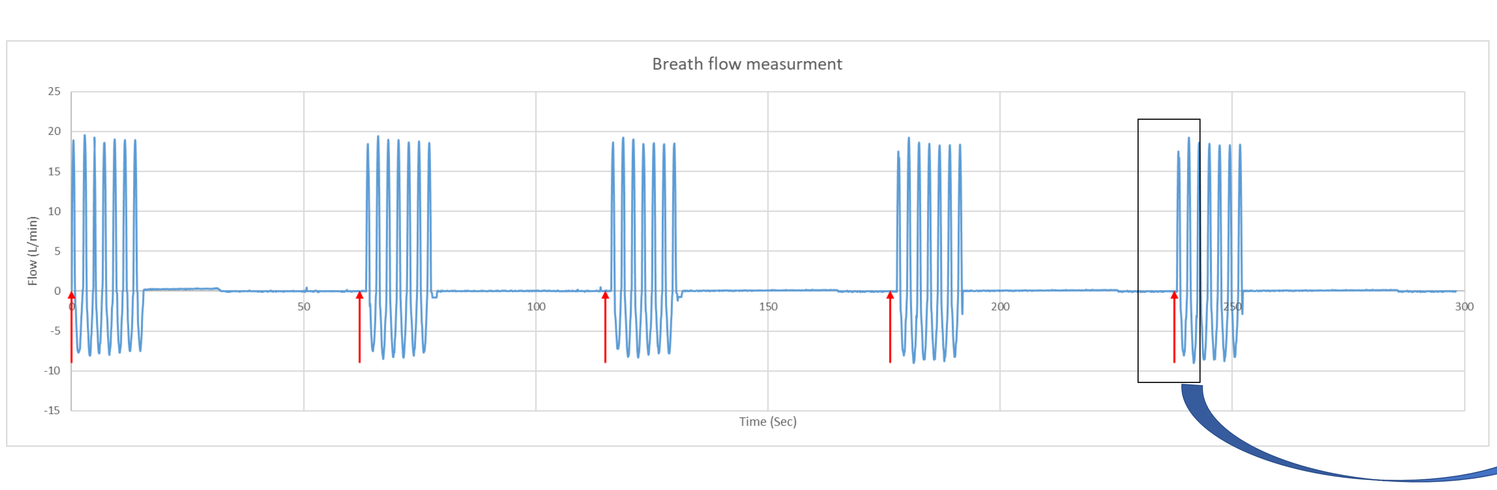
Analyses were performed with pMDI containing salbutamol (Ventolin®, 100 µg per dose, GlaxoSmithKline) and VHC with or without DigitHal® Probe. For IVIVCs, induction port was connected to Breath Simulator (BRS2000, Copley) and the next generation impactor (NGI, Copley) by means of a T-piece. A constant flow of 30 L/min through the NGI was balanced with a pressurized air source of 30 L/min, resulting in simulated tidal breathing through the model and constant air flow through the NGI. To simulate child respiratory flow the settings used were, tidal volume: 100 ml; respiratory frequency: 30 breaths/min; ratio between inspiratory and expiratory time: 1/3. Five actuations were performed with 7 full breathing cycles interval between puffs. Five measurements were made for each set-up. Results are presented as means ± standard deviation. Differences were considered significant at p values <0,05.

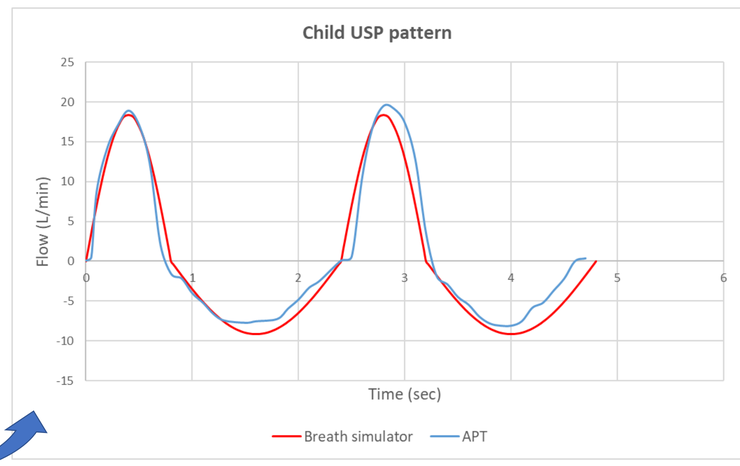


Results

1- Flow analysis

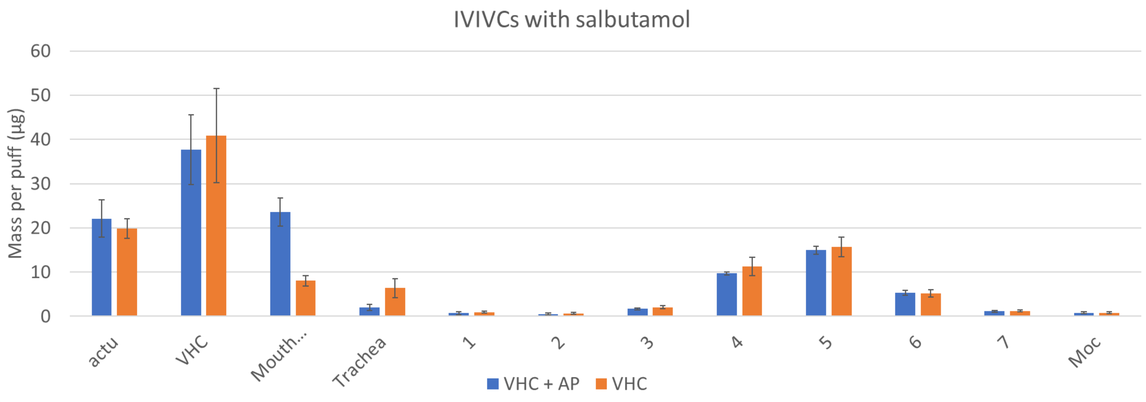
Respiratory profiles generated by the simulator and those recorded by the probe are closely matched. Furthermore, flow rates measured with the probe at maximum inhalation and exhalation (16.01 ± 0.79 and -8.85 ± 0.16 L/min) did not show a significant difference (P>0.05) with simulator values (16.87 and 9.32 L/min) during all experiments, **showing the strong stability of the sensor reading**.





3- Closing ability

Moreover, **no significant difference was found for the mass distribution** of salbutamol for the stage 1 to 8 of the NGI, corresponding to ED (Figure 3) or for FPD, represented by stage 3 to 8 of the NGI. On the other hand, a significant difference between the mouthpiece and the trachea was found. The impaction of bigger particles on the probe may explaine this difference, as well as the lowest amount of drug found in the induction port.



Each stage represents different ranges of particle diameter: d (µm). Stage 1: 11,72 < d; Stage 2: 6,39<d<11,72; Stage 3: 3,99<d<6,39; Stage 4: 2,30<d<3,99; Stage 5: 1,36<d<2,30; Stage 6: 0,84<d<1,6; Stage 7: 0,54<d<0,84.

2-APSD analysis of the Salbutamol

For VHCs including the probe, a slight decrease of the mass median aerodynamic diameter (MMADs), the ED and the fine particle dose (FPD) were noticed, compared to VHC alone. **However, decrease was significant only for the MMAD (p<0.05)**. No significantly change for geometric standard deviation (GSD) or fine particle fraction expressed as % of ED (FPF%ED) were noticed (P>0.05),

	VHC +AP	VHC
Total Dose (µg/puff)	120,15 (±6,11)	112,99 (±7,68)
MMAD (µm)	1,96 (±0,03)	2,03 (±0,08)
GSD	1,67 (±0,04)	1,69 (±0,01)
FPD (µg/puff)	33,60 (±2,03)	36,17 (±5,04)
ED (µg/puff)	34,82 (±2,2)	37,81 (±1,48)
FPF %ED	96,52 (±0,87)	95,60 (±0,70)

MMAD : Mass Median Aerodynamic Diameter; GSD : Geometric Standard Deviation, FPD : Fine particule dose (aerodynamic diameter < 5µm), FPF : Fine particule fraction expressed as % of emitted dose.

Conclusion

Results show that within the scope of our *in vitro* experiments, insertion of DigitHal® probe directly into the mouthpiece of the valve holding chamber **did not affect the particle size** distribution or emitted mass when used in conjunction with a pMDI. It allows a **precise, instantaneous and reproducible measurement of the respiratory flow** regardless of the pMDI actuation. The DigitHal® probe could be used to **improve understanding of patient inhalation when using a VHC**, and potentially be used as an inhalation training aid to help both patients and caregivers.

References :

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