

# Are there differences in throat deposition using variable valved holding chambers?

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## Introduction

Valved holding chambers (VHC) assist patients in their “hand-breathing coordination” by providing a reservoir. Moreover, due to the retention of large aerosol particles, VHCs can effectively reduce throat deposition and therefore topical side effects of steroids.

Non-electrostatic-VHCs additionally feature beneficial effects, e.g.:

- ▶ an increase in delivery of small particles by reducing undesired drug loss to the inner surface of the chamber
- ▶ an improved dose consistency even with variations in delay between MDI actuation and inhalation

In addition the metal non-electrostatic VORTEX<sup>®</sup> (PARI) with its inspiratory cyclone twist principle could improve the aerosol delivery for patients by improving the clearance of the chamber.

## Aim of the study

Most studies about VHCs primarily focus on determining the Fine Particle Dose (FPD) of a specific MDI and VHC combination and disregard measurement of the throat deposition.

Therefore the aim of our study was to examine both the FPD and the throat deposition for non-electrostatic VHCs in comparison to electrostatic VHCs and the MDI alone.

## Materials and Methods

▶ 5 puffs of a HFA-fluticasone MDI (Flutide<sup>®</sup> 125 µg, GSK) were fired at 1 minute interval via a distinct VHC into an Anderson 8-stage impactor in accordance with European Pharmacopoeia (Ph. Eur.) at 28.3 l/min (28.2 ± 2.1°C and 53.3 ± 7% relative humidity). The USP induction port (throat) and each stage of the impactor were eluted and an aliquot was assayed by HPLC and UV detection.

- ▶ Tests were carried out 3 times with 3 VHCs each
- ▶ Statistical analysis was done by ANOVA and t-test (p < 0.05)

| Name / Manufacturer  | Picture   | Volume / Material                   | Non-electrostatic |
|--|---|-------------------------------------|-------------------|
| AeroChamber <sup>®</sup> Plus (AC Plus) for babies / Trudell |  | 145 ml / plastic                    | No                |
| AeroChamber <sup>®</sup> Max (AC Max) for children / Trudell |  | 190 ml / charge dissipative plastic | Yes               |
| Babyhaler <sup>®</sup> / GSK                                 |  | 350 ml / plastic                    | No                |
| Nebuchamber <sup>®</sup> / AstraZeneca                       |  | 250 ml / metal                      | Yes               |
| VORTEX <sup>®</sup> for babies / PARI                        |  | 192.5 ml / metal                    | Yes               |

Table 1: Main characteristics of the five VHCs used in this study

## Results

### Uniformity of Dose Delivery

The uniformity of dose delivery was characterized by a dose unit sampling apparatus according to Ph. Eur. based on 10 puffs Flutide<sup>®</sup> HFA MDI and fired from 3 canisters, each.

It could be shown that the delivery of the three tested MDIs varies only in a range of +/- 6 µg from the mean value (Data not shown).

### Mass Median Aerodynamic Diameter (MMAD)

The MMAD of the aerosol emitted from the fluticasone-MDI alone and from the VHCs (except Babyhaler<sup>®</sup>) is in a range of about 3 µm. The remarkably lower MMAD obtained from the Babyhaler<sup>®</sup> is probably attributed to its large volume (350 ml) leading to an increased adhesion of drug particles to the inner surface of the tube.

|           | MDI alone   | Nebuchamber <sup>®</sup> | AC Max <sup>®</sup> | VORTEX <sup>®</sup> | AC Plus <sup>®</sup> | Babyhaler <sup>®</sup> |
|-----------|-------------|--------------------------|---------------------|---------------------|----------------------|------------------------|
| MMAD [µm] | 3.15 ± 0.46 | 2.99 ± 0.17              | 3.03 ± 0.17         | 3.12 ± 0.18         | 3.06 ± 0.26          | 2.43 ± 0.45            |
| GSD       | 1.55        | 1.36                     | 1.36                | 1.45                | 1.45                 | 1.44                   |

Table 2: MMAD of the MDI alone and in association with the five VHCs

### Fine Particle Dose (FPD)

Fig. 1 shows the FPDs (particles < 4.7 µm) for the five VHCs and the MDI alone. It can be seen that the group of the three non-electrostatic VHCs deliver similar FPD, ranging from 48 µg (VORTEX<sup>®</sup>) up to 54 µg (Nebuchamber<sup>®</sup>) without significant differences within this group.

The two electrostatic VHCs, AC Plus<sup>®</sup> (34 µg) and especially Babyhaler<sup>®</sup> (13 µg), show a significant loss in FPD. This means that on average the group of non-electrostatic VHCs delivers 46% and 161% higher FPD in comparison to AC Plus<sup>®</sup> and Babyhaler<sup>®</sup>, respectively.

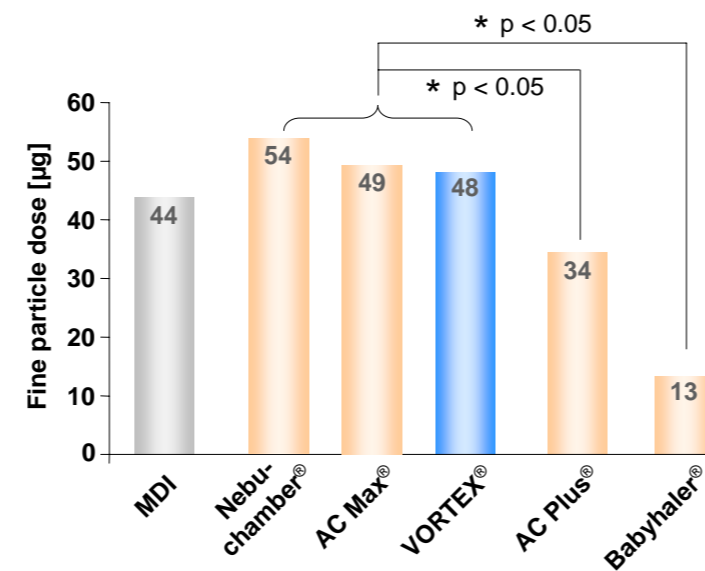


Figure 1: The group of non-electrostatic VHCs deliver significantly the highest FPD in comparison to AC Plus and the Babyhaler (particles < 4.7 µm)

### Throat deposition

As shown in Fig. 2, all tested VHCs reduce oropharyngeal deposition of fluticasone compared with the MDI alone (78 µg). Among the non-electrostatic VHCs, throat deposition for VORTEX<sup>®</sup> was significantly more than 4-fold lower in comparison to Nebuchamber<sup>®</sup> (2.1 vs. 8.7 µg) and more than 2-fold in comparison to AC Max<sup>®</sup> (2.1 vs. 4.4 µg). This effect may be due to the cyclone-twist principle of the VORTEX<sup>®</sup> which may help in the retention of large aerosolized drug particles.

The very efficient reduction in throat deposition by the Babyhaler<sup>®</sup> (0.22 µg) is associated with a more than 3-fold reduction in FPD (13 µg; see figure 1) leading to a possibly suboptimal therapeutic dose.

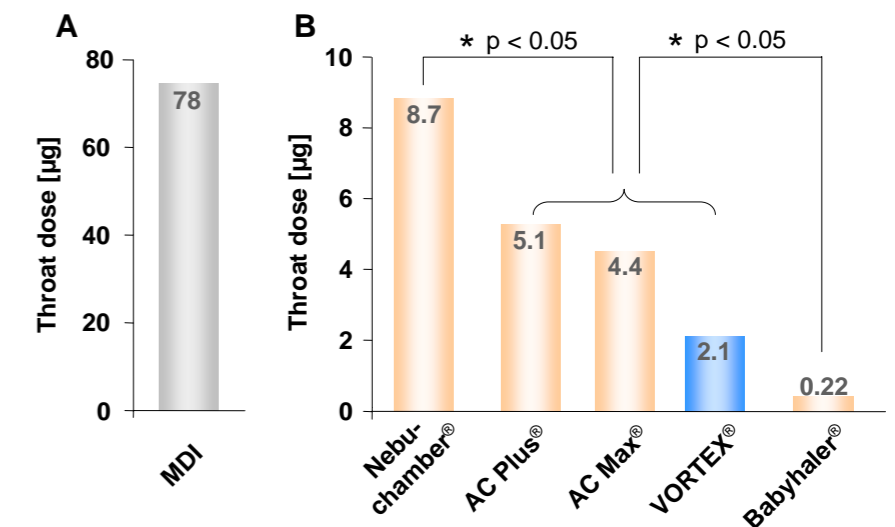


Figure 2: Throat deposition of the MDI alone (A) and with five VHCs (B)

## Conclusion

- ▶ Although the Babyhaler<sup>®</sup> reduces throat deposition, it can be assumed that the very low FPD bears a potential risk of under dosing
- ▶ The high throat deposition of the Nebuchamber<sup>®</sup> negates a primary advantage of VHC use: reduction of oropharyngeal deposition and topical side effects of inhaled steroids
- ▶ Since VORTEX<sup>®</sup> is very effective in reducing throat deposition combined with a high FPD of fluticasone, VORTEX<sup>®</sup> may improve lung targeting most efficiently