In Vitro Comparison of Aerosol Characteristics of Two Pressurized Metered Dose Inhaler Formulations Commonly Used in COPD

M1027


Introduction

The valved holding chamber (VHC) has been designed to help improve and optimize delivery for those using pressurised metered dose inhalers (pMDIs). The OptiChamber Diamond VHC (Diamond, Philips Respironics, Respironics New Jersey, Inc., Parsippany, NJ) is a compact, anti-vest VHC designed to facilitate effective aerosol delivery to respiratory patients. The in vitro aerosol characteristics of two pMDI drug formulations commonly used for the treatment of COPD, HFA albuterol sulfate and HFA ipratropium bromide, were compared using a preproduction Diamond VHC, an AeroChamber Plus Z-Stat (Z-Stat, Monaghan Medical Corp., Plattsburg, NY) VHC and the pMDI alone. The tests were conducted using two flow rates, 30 L/min and 15 L/min.

Method

Figure 1. The OptiChamber Diamond VHC can be used to optimize delivery from pMDIs.

Materials

- 6 x ProAir HFA, 18 µg (shaken 10 min before actuation)
- 6 x Atrovent HFA, 25 µg (shaken 10 min before actuation)
- 6 x AeroChamber Plus Z-Stat (Z-Stat, Monaghan Medical Corp., Plattsburg, NY) VHC and the pMDI alone.

Pre-test conditioning

- Primed 3 x prior to test
- Priming actuations
- Adjusted for test volume
- Washed in warm soapy water, rinsed and air dried
- Dried to ambient conditions
- NGI leak tested
- NGI cups and VHCs were processed using HPLC assay diluent
- Equipment and fluids stabilized

Tests conducted on:
- pMDI alone (n=6)
- pMDI alone (n=6)
- pMDI alone (n=12)
- Z-Stat VHC (n=6)
- Diamond VHC and pMDI with Z-Stat VHC for albuterol
- Diamond VHC and pMDI with Z-Stat VHC for ipratropium bromide

Results

Figure 2. Experimental test method.

After each test the induction port, back-up filter, NGI cups and VHCs were processed using HPLC assay diluent for sprays and aerosols, and 10% acetic acid solution for saliva. The emitted dose (drug entering NGI) fine particle dose (amount of drug in NGI ≤ 4.7 µm), and Mass Median Aerodynamic Diameter (MMAD) were calculated. The equipment was washed and dried after each drug/VHC test.

Figure 3. Emitted dose (drug entering the NGI) from the pMDI alone, pMDI with Diamond VHC, and pMDI with Z-Stat VHC using albuterol. Fine particle dose is highlighted and the dose in particles > 4.7 µm highlighted. Error bars denote standard deviation about the mean.

Figure 4. Emitted dose (drug entering the NGI) from the pMDI alone, pMDI with Diamond VHC and pMDI with Z-Stat VHC using ipratropium bromide. Fine particle dose is highlighted and the dose in particles > 4.7 µm highlighted. Error bars denote standard deviation about the mean.

Discussion

The fine particle dose from the pMDI alone was similar or smaller than from the pMDI VHC combinations, but the emitted dose was higher for the pMDI alone, meaning a greater amount of drug was delivered in larger particles that would be expected to deposit in the throat and upper airways. The aerosol delivery characteristics from the two pMDI VHC combinations were comparable.

Conclusions

- The fine particle dose was higher using a pMDI VHC combination than the pMDI alone for both drugs at the 15 L/min flow rate despite a higher emitted dose from the pMDI alone.
- The emitted dose was higher from the pMDI alone across both drug and flow rate variables.
- The MMAD was higher at the 15 L/min flow rate than the 30 L/min flow rate across both drugs using both the pMDI alone and the pMDI VHC combinations.

References

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