

IN VITRO EVALUATION OF DRUG DELIVERY (MASS) FROM MDIS WITH A BREATH-ACTUATION DEVICE

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BACKGROUND

Metered dose inhalers continue to be widely used by patients despite reported difficulties with their use. Studies show that up to 70% of patients are unable to use their metered-dose inhaler (MDI) correctly (Dolovich, MA et al, CHEST 2005). Much of this failure relates to the patients' inability to coordinate their inhalation with the delivery of the medication from the MDI. As a consequence, patients may not be getting the appropriate dose from the inhaler for management of their disease.

To help patients alleviate this "timing" problem, Respirics is developing a number of devices which function as a result of a patient's inspiratory effort. The company has developed MD Turbo™ (Figure 1), a breath-actuated accessory device, to be used with many of the currently prescribed MDIs.

We evaluated the use of different MDIs in conjunction with various technologies designed to assist with the delivery of aerosolized medications. We compared the amount of drug delivered from three separate MDIs when used alone, with a valved holding chamber (Pocket Spacer™, Ferraris Medical Inc.) and with MD Turbo™.



FIGURE 1: MD Turbo™ shown as manufactured (left) and with a standard MDI loaded inside (right).

OBJECTIVE

To compare the total delivered dose output (micrograms/dose) for three different metered-dose inhalers when used with the Respirics MD Turbo™, the Pocket Spacer™ and the MDI boot supplied with the medication.

MATERIALS AND METHODS

Three different MDIs, albuterol USP (Warrick Pharmaceuticals), Alupent® (metaproterenol sulfate, Boehringer Ingelheim) and Flovent® (fluticasone propionate, GSK) were tested by attachment to a throat model, feeding into a filter connected to a Harvard breathing machine (Harvard Apparatus Dual Phase Control Respirator Pump, Harvard Apparatus, South Natick MA). See Figure 2 below.

Each MDI was tested on the circuit by attachment to an adapter at the throat model under three different configurations: Alone (canister in boot as supplied by manufacturer), with a valved holding chamber and then with the MD Turbo™. Each MDI was tested (n=10 actuations), with the drug delivered at the start of inhalation. The Harvard breathing machine, which inhaled and exhaled through the circuit, was turned on and set at 5 breaths per minute with a tidal volume of 750 mL. Each filter was capped and rinsed with solvent to collect all deposited drug. The liquid was then analyzed by HPLC.

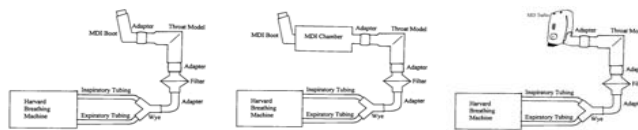


FIGURE 2: Test setups shown with MDI alone (left), MDI attached to a holding chamber (middle) and MDI inside the MD Turbo™ (right).

RESULTS

The mass of drug delivered with use of the MD Turbo™ was comparable to the amount delivered by the MDI on its own in the case of all three drugs. With use of the Pocket Spacer™, the amount of drug delivered was significantly reduced in the cases of albuterol and metaproterenol. The differences between devices were considered to be statistically significant if $p < 0.05$.

	MDI + MD Turbo™ ($\mu\text{g} \pm \text{SD}$)	MDI + Pocket Spacer™ ($\mu\text{g} \pm \text{SD}$) (p value)	MDI Alone ($\mu\text{g} \pm \text{SD}$) (p value)
Albuterol	27 \pm 3	21 \pm 3 (0.0002)	28 \pm 2 (0.76)
Metaproterenol sulfate	124 \pm 36	67 \pm 10 (0.0005)	150 \pm 35 (0.12)
Fluticasone propionate	37 \pm 5	32 \pm 4 (0.05)	40 \pm 4 (0.2)

Table 1: Study results for albuterol, metaproterenol and fluticasone MDIs for all three test configurations.

DISCUSSION

The mass of drug delivered (collected on the filter) by MDI alone and with use of the MD Turbo™ was comparable for all three drugs. In the case of the Pocket Spacer™, however, the amount of drug collected on the filters was significantly less than that with use of the MD Turbo™ for two of the three drugs tested ($p < 0.05$). This is consistent with the use of a spacer which enables separation of larger drug particles from the aerosol spray which might otherwise impact a user's throat.

In every case, the amount of drug collected when the Pocket Spacer™ was used was less than with the other delivery methods. In the case of metaproterenol, there was significantly less drug collected on the filters (67 mcg of a nominal dose of 650 mcg, 10.3%). The particle size of the drug expelled from the MDI was much larger as measured by MMAD than that of the other two drugs (4.64 μm vs. 1.80 μm and 2.26 μm). For this reason, these particles were more likely to deposit on the inside of the chamber due to gravity. The drug that settled within the chamber did not enter the breathing circuit and therefore could not be captured by the filter.

With the built-in breath actuation trigger and an integrated dose counter, the MD Turbo™ should offer a portable, valuable accessory device for patients unable to otherwise coordinate the delivery of medication from their inhaler with their inspiratory breath.

CONCLUSION

The amount of drug delivered from three MDIs was not significantly decreased with the use of the MD Turbo™. We conclude that the MD Turbo™ can accommodate a variety of MDIs, and can assist with the delivery of those aerosolized medications without any significant decrease in the dose of medication delivered.