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DDL 2020
Drug Delivery to the Lungs

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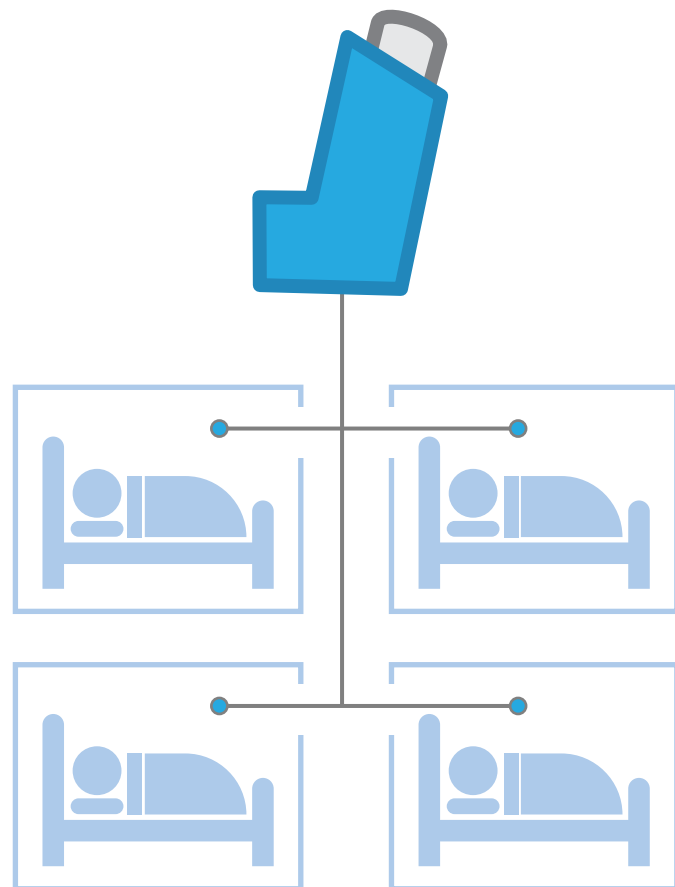
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A Laboratory Study to Evaluate a Pressurized Metered Dose Inhaler with Valved Holding Chamber Use Scenario in a COVID-19 Situation where pMDIs in Short Supply

BACKGROUND

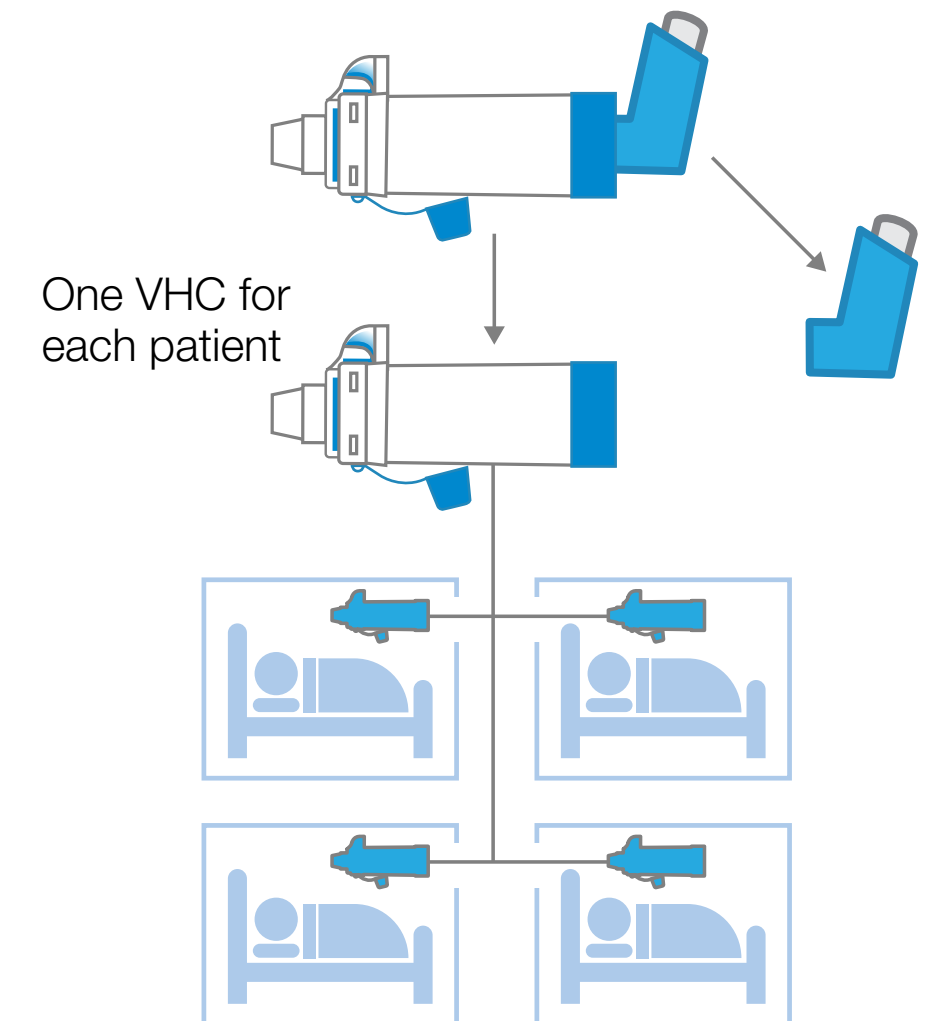
- Patients infected with COVID-19 and admitted to hospital often require inhaled bronchodilator therapy to manage breathlessness.
- Some US hospitals are considering new ways to deliver such medication with Pressurized Metered Dose Inhalers (pMDIs) in short supply
- One approach to inhaler management is often referred to as the “common canister” protocol: one pMDI used to treat several patients
- Keeping the inhaler segregated from the patient is essential, thereby allowing for reuse elsewhere without risk of contamination



The “Common Canister” protocol.

A Potential Solution

- Valved Holding Chambers (VHC) are widely used with pMDIs to improve aerosol delivery to the lungs:
 - Remove coarse particle fraction and avoid need for coordinating onset of inhalation with inhaler actuation
- Why not use the VHC to transport the emitted aerosol to the patient from the inhaler located remotely? (with the pMDI removed after actuation)
- A US hospital approached our laboratory with a proposal to actuate multiple times into the VHC outside of the patient's room, remove the pMDI, and take the VHC alone to the patient for inhalation...would this work?
- Aim of study:
 - Hospital interested in finding out how to maximize the delivered dose of salbutamol in a single treatment – i.e. what is the relationship between number of actuations and emitted mass. The original proposal from hospital had been to actuate 4 times in rapid succession



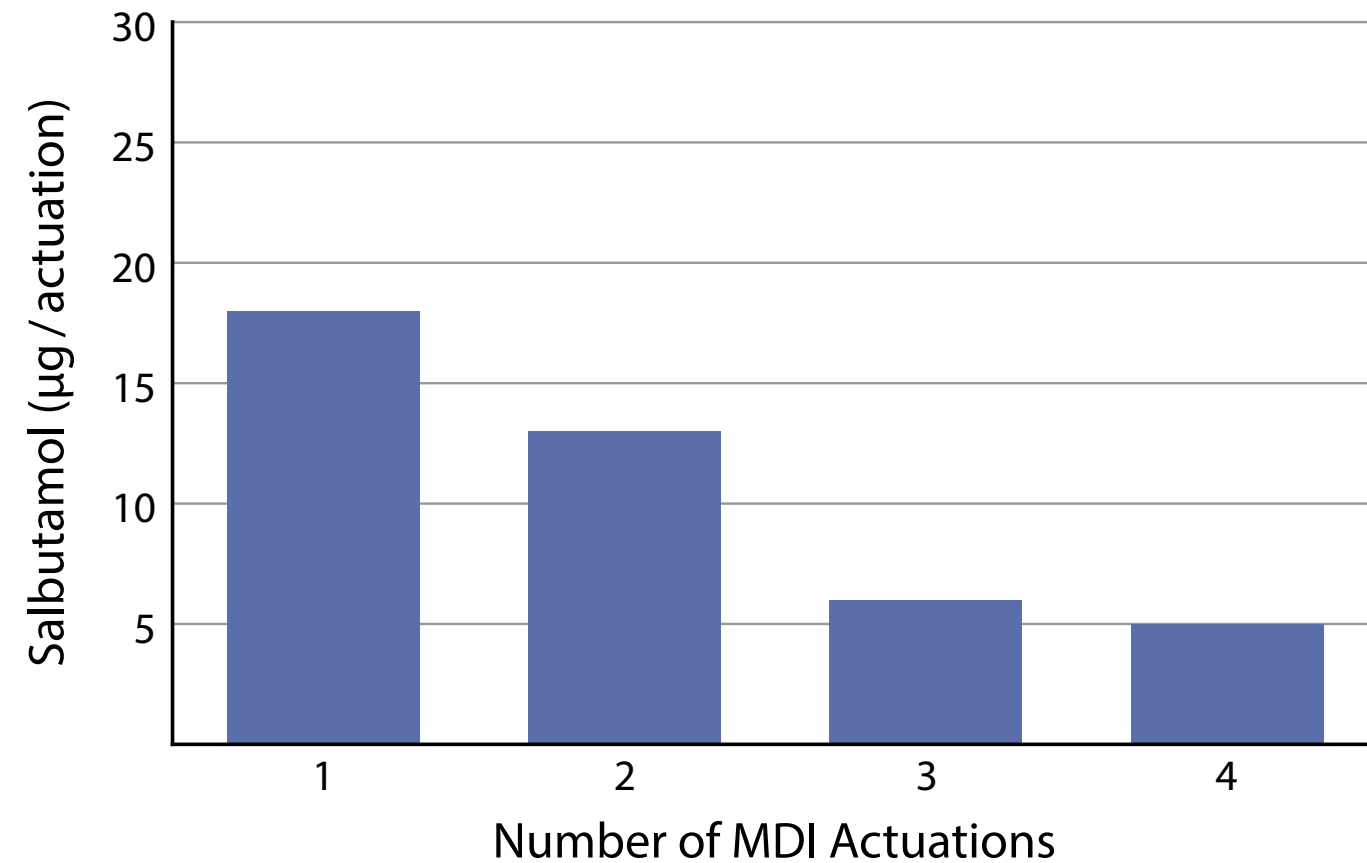
Covering pMDI actuator port of VHC protects medication from escape during transfer to patient

METHODS

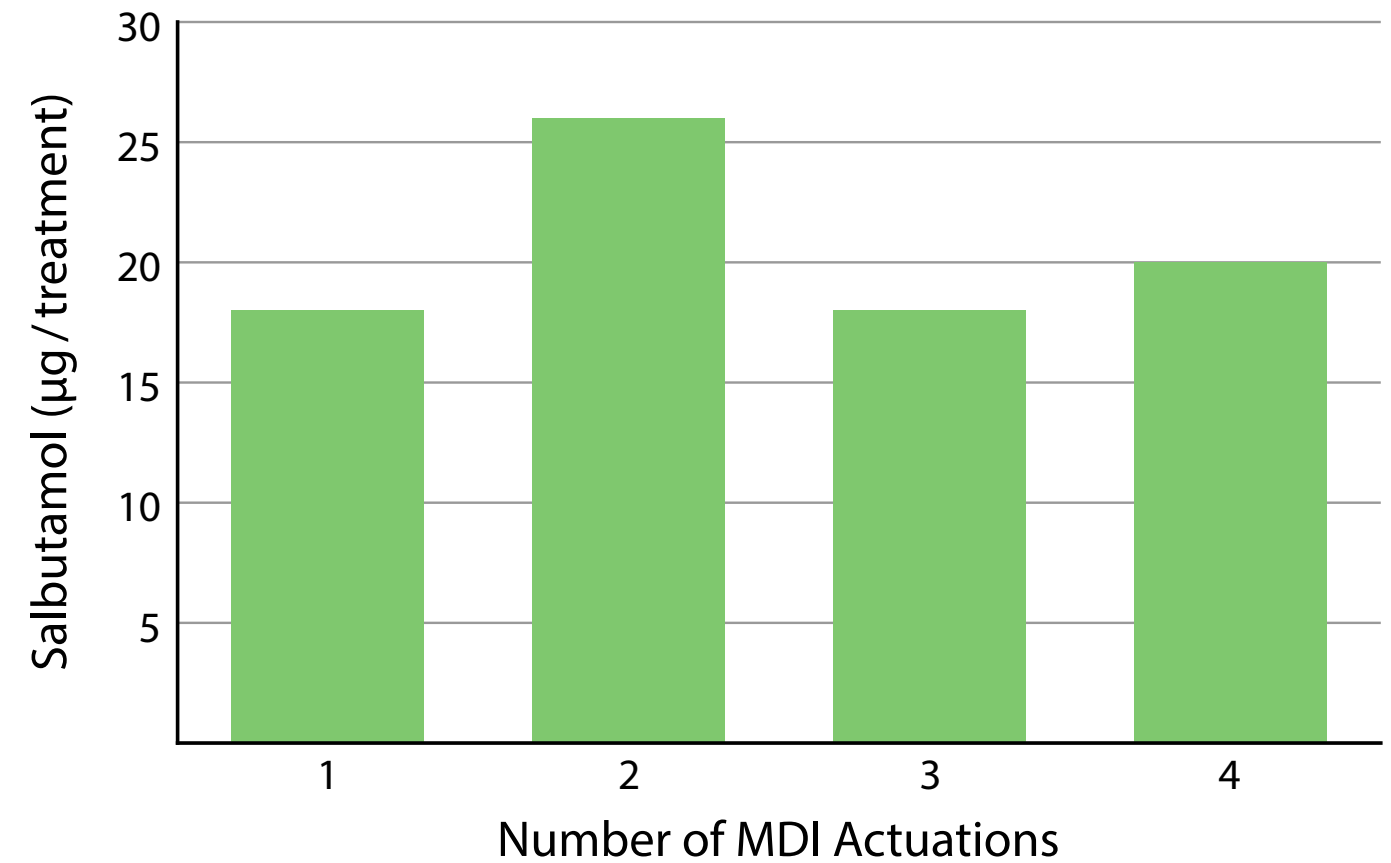
- A demonstration pMDI (Ventolin[†], 100 µg/actuation salbutamol) was actuated once into a VHC (antistatic **AeroChamber Plus* Flow-Vu***), simulating use at the medication cart in a hospital hallway
- The inhaler was removed and the pMDI adapter port of the VHC covered
- 10 seconds elapsed (delay) before connecting the VHC mouthpiece to a vacuum via an electrostatic filter to collect the suspended aerosol at 28.3 L/min.
 - This delay simulated the time to enter patient room, and have patient inhale the salbutamol.
- Two, three and four rapid actuations (1-s apart) into the VHC prior to administration were also simulated (off label use).
- The mass of salbutamol emitted was determined by HPLC-spectrophotometry.

RESULTS

Delivered Dose of Salbutamol Per Actuation



Delivered Dose of Salbutamol Per Treatment



- Almost all this mass was known to comprise fine particles $< 5 \mu\text{m}$ aerodynamic diameter from previous measurements made by cascade impactor

DISCUSSION

- Not surprisingly, it was confirmed that the standard (per label) practice of actuating and inhaling one puff at a time is the most efficient delivery method
 - Rapid consecutive actuations is likely to chill MDI metering valve, increase friction, and reduce delivery
 - Rapid consecutive actuations also has the potential to increase retention of drug within the chamber
- However, for this specific and off-label delivery scenario that was being proposed by the US hospital, the maximum amount delivered as a single dose was achieved following two rapid actuations and as such can be considered optimal
- Less than or more than two actuations resulted in lower total delivery of salbutamol

CONCLUSIONS

- The most efficient and effective delivery method remains that recommended in the device IFU (one actuation inhaled at a time, as well inhalation as soon as possible after actuation)
- However, this laboratory-based study has indicated that a modified common-canister protocol with an anti-static VHC as the aerosol transfer vehicle has the potential to be a viable 'off-label' proposition in hospital situations where there is an urgent need to conserve pMDI medication as well as avoid cross-contamination from pathogenic viruses or bacteria