

In Vitro Comparison of Albuterol Dose Output for Standard MDI with LiteAire Spacer versus Misty Max 10 Nebulizer

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Abstract

Background: Though there is a tremendous variability in number of MDI actuations (2-12) used in studies comparing beta agonist delivery via MDI/spacer and a nebulizer, literature supports the use of 6 MDI actuations. As delivery systems may influence dose output, prior to conducting a clinical efficacy comparison study, it would be prudent to determine the in vitro dose outputs using the two systems.

Objective: The purpose of this study was to perform an in-vitro B-agonist dose output comparison between 6 actuations of “MDI with LiteAire Spacer” versus 1 Unit dose with a “Nebulizer”.

Method: A Standard MDI/LiteAire Spacer combination and Nebulizer were tested using the Michigan Instrument Dual Test Lungs driven by a Puritan Bennett 7200 ventilator set at 14 breaths/minute, TV of 600 ml and I:E ratio of 1:4. The LiteAire was tested with 6 MDI actuations, one puff/respiratory cycle and the Nebulizer with one 3-ml vial (0.833mg/ml) Albuterol Solution. Nebulization with oxygen (8L/min) was run (sputtering time) for five minutes. Each dose deposition filter was washed with 0.05mM KCl with 1% acetic acid buffer and samples were analyzed by UV spectrophotometer, at a wavelength of 276nm ±1nm to calculate the total dose output. The above experiment was repeated for a total of three times (N=3) for both devices.

Results: The average total dose output ± Standard Deviation was 176 ± 27 micrograms for 6 puffs of MDI/LiteAire Spacer versus 220 ± 14 micrograms for Nebulizer (p value 0.067), respectively.

Conclusion: We recommend using 6 albuterol MDI actuations with LiteAire spacer, when conducting a clinical efficacy study as the in vitro dose outputs using 6 MDI actuations and a unit dose of nebulizer are comparable. We cannot comment on effective Respirable dose output equivalency as particle size distribution studies were not conducted.

Introduction

The purpose of this study was to perform an in-vitro B-agonist dose output comparison between 6 actuations of an MDI with LiteAire Spacer versus 1 Unit dose with a Nebulizer. The total dose output in micrograms using Standard MDI Boot and a LiteAire Spacer Device for albuterol (CFC) (Inhalation Aerosol – IVAX Pharmaceuticals, Inc.) is determined using 6 actuations of medication versus a Misty Max-10 Nebulizer treatment using one unit dose of albuterol sulfate. The amount collected on the filter (AireLife Nonconductive Respiratory Therapy Filter, Bacterial/Viral Retentive) is the total amount of active ingredient (albuterol/albuterol sulfate) summed over all particle sizes which would be delivered to a patient.

A Standard MDI/LiteAire Spacer combination and Nebulizer were tested using the Michigan Instrument Dual Test Lungs driven by a Puritan Bennett 7200 ventilator set at 14 breaths/minute, TV of 600 ml and I:E ratio of 1:4. The LiteAire was tested with 6 MDI actuations, one puff per respiratory cycle and the nebulizer with one 3-ml vial (0.833mg/ml) albuterol solution. Nebulization with oxygen (8L/min) was used for five minutes.

Method.

The LiteAire spacer device is used as shown in Fig 1. The LiteAire spacer device is connected to a USP standard aluminum throat model. A filter (Airlife Nonconductive Respiratory Therapy Filter, Bacterial/Viral Retentive) traps the particles on the opposite side of the throat. The flow is created by one lung of a Dual Adult Test Lung while the opposite lung is driven by a Michigan Instrument Dual Test Lungs driven by a Puritan Bennett 7200 ventilator set at 14 breaths/minute, TV of 600 ml and I:E ratio of 1:4. The LiteAire was tested with 6 MDI actuations of albuterol (CFC) (IVAX Pharmaceuticals, Inc.)

For the Misty Max-10 Nebulizer See Fig 2. An oxygen tank is used to power the Misty Max-10 Nebulizer using standard Nebulizer tubing and is connected to a T-connector where one end of the T-connector is left open and the other end is connected to USP standard aluminum throat model. A filter (Airlife Nonconductive Respiratory Therapy Filter, Bacterial/Viral Retentive) traps the particles on the opposite side of the throat. The flow is created by one lung of a Dual Adult Test Lung while the opposite lung is driven by a Michigan Instrument Dual Test Lungs driven by a Puritan Bennett 7200 ventilator set as above. The Nebulizer was used with one 3-ml vial (0.833mg/ml) albuterol solution. Nebulization with oxygen (8L/min) occurred for five minutes.

At the end of the simulated treatments each dose deposition captured by filter was washed with 0.05mM KCl with 1% acetic acid buffer and samples were analyzed by UV spectrophotometer, at a wavelength of 276nm ±1nm to calculate the total dose output. The above experiment was repeated for a total of three times (N=3) for both treatment modes.

Results

Experimental Run albuterol / albuterol sulfate	LiteAire Dose output of Albuterol in ug per Treatment (One Treatment = six actuations)	Misty Max-10 Dose output of Albuterol Sulfate in ug per Treatment
1	161.540	204.528
2	159.143	230.496
3	207.082	224.503
Average Total Dose Output	175.922± 27.013	219.842± 13.597

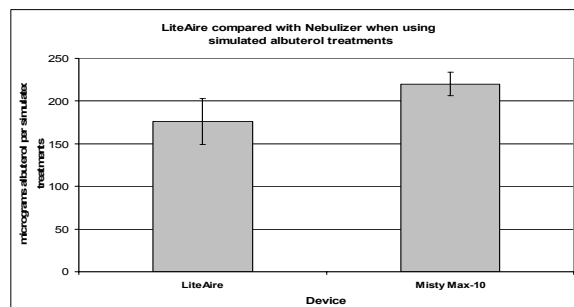


Fig 1: Setup with LiteAire Spacer Device

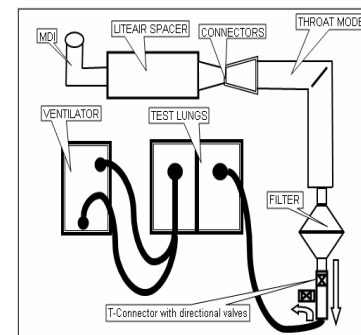
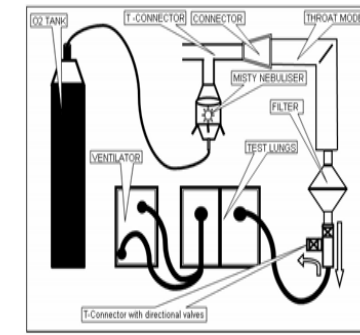


Fig 2: Misty Max-10 Nebulizer



Conclusion

We recommend using 6 albuterol MDI actuations with the LiteAire spacer when conducting a clinical efficacy study as the in vitro dose outputs using 6 MDI actuations and a unit dose of nebulizer are comparable. However, a controlled study comparing the two modes of treatment in patients with asthma would be desirable to demonstrate equivalent clinical efficacy.