In Vitro Comparison of a Novel Nebulizer with Ultrasonic and Pneumatic Nebulizers

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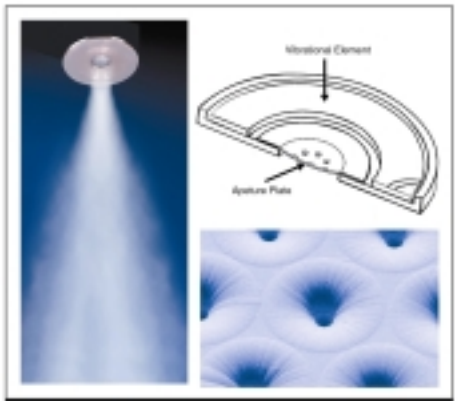
Abstract:

Nebulizers vary in the amount of inhaled drug and the time required to administer a treatment. The lower the inhaled dose and the longer the time of administration, the less likely the patient will be to adhere to the prescribed treatment plan.

The Aerogen Aeroneb® 3 Nebulizer (Figure 1; in development) is a compact nebulizer utilizing Aerogen's OnQ™ aerosol generator, consisting of a domed aperture plate with precision-formed holes and a vibrational element which creates a micro-pumping action producing fine-particle, low-velocity aerosol using no propellants or compressors (Figure 2). Aerosol particle size, output rate and fine particle fraction are functions of the aperture hole exit diameter. We wanted to determine how this novel nebulizer compared to a range of commercially available ultrasonic and pneumatic nebulizers.

FIGURE 1. THE AERONEB® 3 NEBULIZER

FIGURE 2. AEROGEN ONQ AEROSOL GENERATOR WITH DIAGRAM OF AEROSOL GENERATOR COMPONENTS (TOP RIGHT), MICROSCOPIC VIEW OF APERTURE PLATE (BOTTOM RIGHT) AND PICTURE OF AEROSOL GENERATOR (LEFT).



Methods:

We compared the inhaled mass and performance characteristics of three ultrasonic nebulizers (Omron MicroAir®, Mabis Mist™, and Puritan Bennett Easy Neb™) and three compressor-driven pneumatic nebulizers (Omron CompAir Elite®, DeVilbiss Model 800™, Pari LC Plus®) to a prototype nebulizer (Aerogen Aeroneb® Go). Each nebulizer was filled with 2.5 mg (3 mL of 0.083%) albuterol sulfate. Drug was collected on filters placed between the nebulizer and a breath simulator modeling an adult breathing pattern (Vt 500 mL, rate 15, and 0.35 duty cycle) (Figure 3). The amount of drug deposited on the filter (Inhaled Mass) was determined for each device (n=3). Drug was eluted from the filter and determined by reverse phase HPLC with isocratic elution and UV detection at 275 nm. Flow rate (mL/min) of emitted aerosol, and residual volume (mL) remaining in the nebulizer were determined gravimetrically. Treatment time to end of dose or sputter was recorded. Volume Median Diameter (VMD) was determined by laser diffraction using a Malvern Spraytech™.

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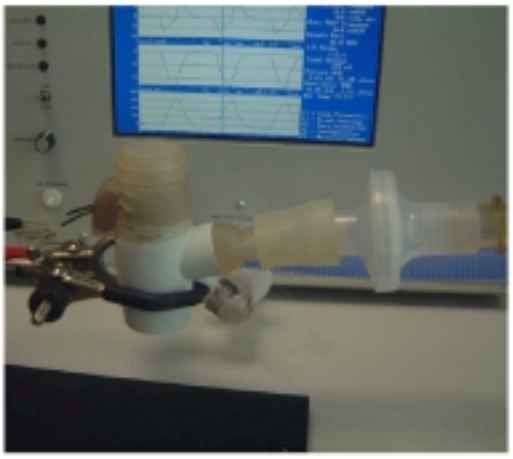
FIGURE 3. THE *IN VITRO* MODEL, SHOWING A NEBULIZER (AERONEB GO) ATTACHED TO A FILTER AND LUNG SIMULATOR (HANS RUDOLPH) ADJUSTED TO ADULT TIDAL BREATHING PARAMETERS.



Results:
Test results are shown in Table 1 below. Inhaled mass is expressed as the percent of total dose delivered to the filter for each nebulizer (n=3).

TABLE 1: COMPARISON OF DEPOSITED DOSE OF ALBUTEROL SULFATE (INHALED MASS), FLOW RATE, TIME OF ADMINISTRATION, RESIDUAL VOLUME AND VOLUME MEDIAN DIAMETER (VMD) WITH 7 NEBULIZERS. NEBULIZER TYPES INCLUDE ELECTRONIC MICROPUMP (EM), ULTRASONIC (USN), AND PNEUMATIC (PN).

Devices	Inhaled Mass (%)	Output Rate (mL/min)	Time (min)	Residual (mL)	VMD (μm)	Type
Aeroneb 3	45	0.49	6.1	0.1	4.9	EM
Omron Micro Air	55	0.21	13.3	0.3	7.8	USN
Mabis Mist	21	0.09	16.6	1.5	4.4	USN
Puritan Bennett Easy Neb	29	0.30	6.0	1.4	4.8	USN
Omron Comp Air Elite	34	0.24	7.1	1.4	9.7	PN
DeVilbiss 800	10	0.20	5.9	2.1	5.4	PN
Pari LC Plus	17	0.21	7.9	1.5	4.8	PN

Discussion: The Aeroneb 3 (in development) and the Micro Air had the lowest residual drug volumes (<0.3 mL) and delivered more inhaled mass than the other nebulizers tested, however the Micro Air required greater than two fold the treatment time. The flow rate of emitted aerosol was greatest with the Aeroneb Go. The ultrasonic nebulizers had a wider range of variability in flow rates (0.09 – 0.30 mL/min), than the pneumatic nebulizers (0.20 – 0.24 mL/min). Treatment time for all nebulizers ranged from 5.8 – 13.3 minutes.

Conclusion: The Aerogen Aeroneb 3 prototype nebulizer performed as well or better than the ultrasonic and pneumatic jet nebulizers tested.