Technology Review and Performance Report for the Aeroneb® Professional Nebulizer System

Overview

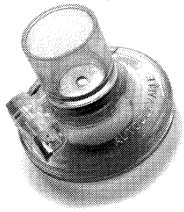
The purpose of this bulletin is to introduce Aerogen's new pulmonary drug delivery system, to describe its operation, and to characterize its performance.

Product Description

The Aeroneb® Professional Nebulizer System (Aeroneb Pro) is a multiple patient use medical device that aerosolizes physician-prescribed solutions for inhalation to patients (infants through adults) requiring positive pressure breathing assistance, including mechanical ventilation, as well as hand-held nebulizer therapy. The System operates inline with standard ventilator circuits and mechanical ventilators, and also independently with standard aerosol masks and mouthpieces. The Aeroneb Pro has been designed to overcome the limitations associated with pulmonary drug delivery in the acute care environment.

The operational components of the System are:

Nebulizer Unit
(incorporating Aerogen's aerosol generator)



Control Module

Aerogen

Operating Characteristics: The Aerosol Generator

The Aeroneb Pro utilizes Aerogen's aerosol generator, (Figure 1) which operates using a novel mechanism that is unlike any method of aerosolized drug delivery currently available. The aerosol generator consists of a vibrational element and aperture plate with precisely formed holes (Figure 2). During operation, the Control Module drives the vibrational element to create a micro-pumping action that draws solutions in contact with the concave surface of the plate and through the apertures (see arrows in Figure 3) to produce a fine-droplet, low-velocity aerosol. The resulting aerosol is tailored to optimize lung deposition, and has a particle size of 2.1μm MMAD and a GSD of 2.2.

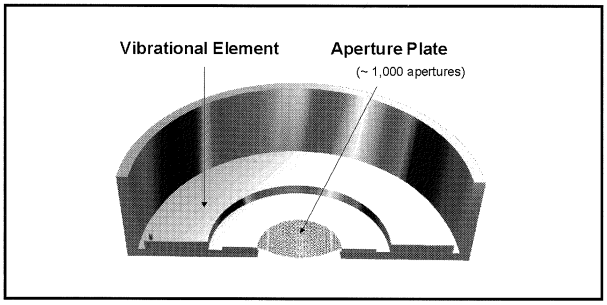


Figure 1: Aerogen Aerosol Generator

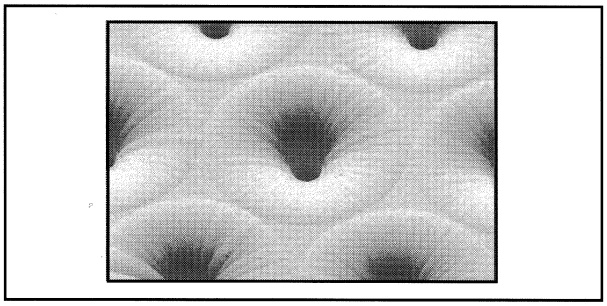


Figure 2: Microscopic View of Apertures (Approx. 1,000 on aperture plate)

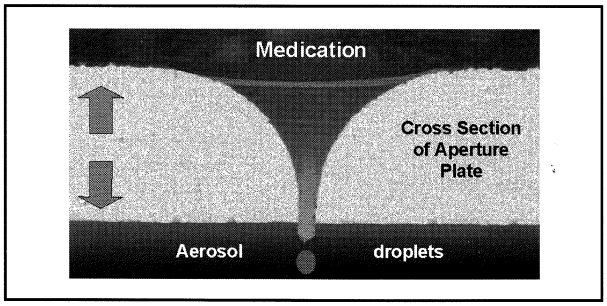


Figure 3: Micro-pumping Demonstration

Aerosol Characteristics

Particle size is a leading factor in determining the fine particle fraction (FPF) of aerosol that travels past the endotracheal tube (of patients on mechanical ventilation) and enters the lungs. FPF directly correlates to the particle fraction that deposits in the various sections of the lungs. An Andersen Mark II Cascade Impactor was used to measure the particle size of the aerosol generated by the Aeroneb Pro. Cascade impaction measures the mass of drug deposited onto plates that collect only particles of a specific size range. GSD and FPF were determined by laser diffraction with the Malvern Spraytech™.

- **MMAD** – Mass median aerodynamic diameter is a descriptor of aerosol size.

  During mechanical ventilation, aerosols with MMADs of 1-3 μm are more likely to achieve greater deposition of medication in the lower respiratory tract since larger particles impact on the ventilator circuit and endotracheal tube, with relatively few particles larger than 2μm delivered beyond the endotracheal tube.[1]

- **GSD** – Geometric standard deviation is used to describe the spread (width of the size distribution) of the aerosol particles. For example, an aerosol with identically sized particles has a GSD of 1.0.

- **FPF** – Fine particle fraction or respirable fraction is the fraction of aerosol containing particles < 5μm. FPF is used to describe the quality of an aerosol and its potential for delivery to the lower respiratory tract.[2]

The Aeroneb Pro aerosol was characterized with the following results: MMAD was 2.1μm, GSD was 2.2 and the fraction of particles smaller than 5μm was 83%.[3]

Output Characteristics

The aerosol output rate from nebulizers, both pneumatic and ultrasonic, is directly affected by the inspiratory flow rate through the ventilator circuit. Nebulizer output also changes with medication fill volume.[4]

In a bench study, aerosol output (using 0.083% albuterol sulfate) from the Aeroneb Pro was evaluated by gravimetric analysis with measured flow of air through the nebulizer tee at 6, 30, and 60 L/min. Aerosol flow measurements were made over time, as medication volumes decreased from 10 to 1 mL at the 6 and 30 L/min flows. Results from the experiment are shown in bold below. The aerosol output was consistent over the range of medication volumes (1 to 9 mL) in the device at 6 or 30 L/min.[5]

Over inspiratory flow rates of 6, 30 and 60 L/min the aerosol output was consistent at approximately 0.4 mL/min.

Effect on Medication Temperature

In ultrasonic nebulizers the transducers convert ultrasonic energy to mechanical energy and generate heat that can be absorbed by the medication.[4] In order to determine whether the micro-pumping action of the Aerogen aerosol generator resulted in any changes in medication temperature during operation, and to distinguish the novel aerosolization technique from ultrasonic nebulizers, the following study was carried out.

10 mL of albuterol sulfate solution were placed in the medication reservoir, and its temperature was measured with a digital thermistor that was placed into the reservoir; ambient temperature was measured to be 23 ± 1° C. The nebulizer was placed into the inspiratory limb of a standard adult ventilator circuit, set to standard adult parameters, and the temperature of the solution was measured at two-minute intervals until the reservoir was empty.

During operation, no significant increase in medication temperature was recorded.

Residual Volume

Also known as dead volume, this is the amount of medication that remains in the nebulizer and is not made available to the patient. Residual volumes in pneumatic and ultrasonic nebulizers vary by model, but generally average 30% of the nominal dose, with a range of 20-50% of the nominal dose. Residual volume in the Aeroneb Pro was measured gravimetrically after nebulization was completed.

The amount of residual medication remaining in the nebulizer after nebulization was complete ranged from 0.2 - 0.4 mL.

Effect on Ventilator Parameters

To determine whether nebulizer operation and opening the medication reservoir (while inline) impact ventilator parameters during mechanical ventilation, peak inspiratory pressure and delivered tidal volumes were monitored before, during and after nebulizer operation. The Aeroneb Pro was placed into a broad spectrum of ventilator circuits and the parameters were representative of adult, pediatric and neonate patients. Albuterol sulfate was used as the delivered drug, and the following is a list of the ventilators tested:

VIP Bird®
VIP Bird® Gold
Draeger Evita 4
Hamilton Galileo®
Puritan Bennett (PB) 840™
PB 760™
PB 7200ae™
Sensormedics 3100A™ Oscillator
Siemens 300
Siemens Servo 900C

There was no discernible change in airway pressure, delivered volume or plateau pressure when the Aeroneb Pro was nebulizing, turned off, or the medication reservoir was open or closed.

Aerosol Delivery During Mechanical Ventilation

To determine the amount of aerosol delivered during mechanical ventilation, the Aeroneb Pro was filled with 3 mL of albuterol sulfate (0.083%) and operated in the inspiratory limb of a standard ventilator circuit with active heated humidification (See Figure 4). The Aeroneb Pro was placed just prior to the wye in the adult and pediatric circuits, and approximately 12 inches back from the wye in the neonatal circuit. The aerosol was delivered into the circuit, and albuterol was collected on an absolute filter distal to the endotracheal tube. The medication is shown as mg of albuterol and the % of nominal dose (% dose) (See Table 1).

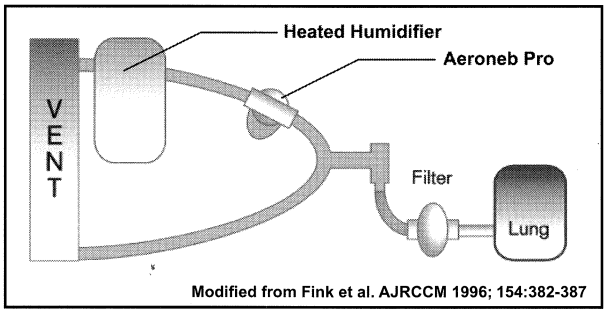


Figure 4: Mechanical Ventilation Model

Parameter Range	Peak Flow L/min	Rate bpm*	Tidal Volume mL	Aeroneb Pro	
				µg	% Dose
Adult	60	12	800	315	13
Pediatric	30	12	300	448	18
Neonatal	6	40	50	87	3

*breaths per minute

Table 1: Aeroneb Pro in vitro drug deposition

References

[1] Fink JB, Dhand R. Aerosol Therapy, in Fink JB, Hunt G, eds. Clinical Practice in Respiratory Care: Philadelphia. Lippincott Raven; 1998.

[2] Dolovich MA. Influence of inspiratory flow rate, particle size, and airway caliber on aerosolized drug delivery to the lung, Respiratory Care 2000; 45(6): 597-608.

[3] Fink JB, and Schmidt D. In vitro comparison of nebulizers for aerosol delivery during mechanical ventilation; ATS 98th International Conference, May 2002.

[4] Hess DH. Nebulizers: principles and performance, Respiratory Care 2000; 45(6): 609-622.

[5] Fink JB, Schmidt D, Power J. Comparison of a nebulizer using a novel aerosol generator with a standard ultrasonic nebulizer designed for use during mechanical ventilation; ATS 97th International Conference, May 2001.

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