

AEROSOL DELIVERY DURING MECHANICAL VENTILATION WITH HIGH FREQUENCY OSCILLATION: AN *IN VITRO* EVALUATION

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INTRODUCTION

Mechanical ventilation with High Frequency Oscillation (HFO) has emerged as an effective method to provide ventilatory support to a population of severely ill patients (Figure 1). While aerosol delivery during mechanical ventilation with HFO has long been considered impractical, the impact of this mode of ventilation on aerosol delivery is not well understood. Aerosol delivery from jet nebulizers during conventional volume- and pressure- limited mechanical ventilation has been limited to less than 3%; however, early reports with HFO indicate substantially less aerosol delivered than with conventional ventilation.



Figure 1. Sensormedics high frequency oscillator.

We wanted to determine whether a novel nebulizer under development for use with mechanical ventilators could reliably deliver a substantial proportion of a nebulized dose of albuterol during ventilation with HFO to a simulated pediatric patient. The Aeroneb™ Professional Nebulizer System (Aeroneb Pro; Aerogen, Inc. – Figure 2) uses an aerosol generator (Figure 3) that consists of a domed aperture plate with precision-formed apertures of a discrete shape and size and a vibrational element to generate a micro-pumping action that creates a fine-droplet, low-velocity aerosol without propellants or compressors that can alter ventilator performance.



Figure 2. The Aeroneb™ Professional Nebulizer System (under development).

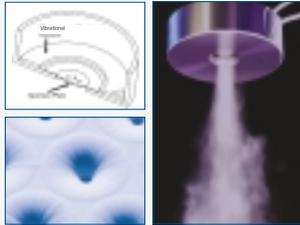


Figure 3. Aerogen's aerosol generator with diagram of aerosol generator components (top left), microscopic view of aperture plate (bottom left) and picture of aerosol generator (right).

METHODS

We compared the ability of the Aeroneb Pro and two small volume jet nebulizers, MistyNeb (Allegrance) and Vix One (Westmed), to deliver 2.5 mg of 0.083% albuterol sulfate to a simulated pediatric patient during mechanical ventilation with high frequency oscillation.

A pediatric test lung was ventilated by a Sensormedic 3100A Oscillator with a heated humidifier (Hudson/RCI) through a 5.0 mm endotracheal tube (Figure 4). The ventilator was set to deliver a frequency of 8.0 Hz, inspiratory time of 33%, amplitude of 25 units and mean airway pressure of 20 cm H₂O. Albuterol was collected with an absolute filter at the distal tip of the endotracheal tube and assayed by HPLC.



Figure 4. Nebulizer setup in oscillator circuit.

All nebulizers were operated with a fill volume of 3 ml of 0.083% albuterol sulfate (2.5 mg), and both jet nebulizers were operated with 6 L/min of oxygen. Nebulizers were run until sputter (jet), or end of aerosol generation (Aeroneb Pro). Ventilator parameters were recorded before and during nebulization for each device. Operation of the ventilator was monitored during refilling of the nebulizers, initiation of nebulization and discontinuation of nebulization. All experiments were repeated in triplicate, with data reported as mean ± standard error (Figures 5 and 6).



Figure 5. Aeroneb Pro in oscillator circuit.



Figure 6. Jet nebulizer in oscillator circuit.

RESULTS

The Aeroneb Pro delivered more albuterol (582 ± 89 µg) to the end of the endotracheal tube than the MistyNeb (201 ± 87 µg) or the Vix One (197 ± 50 µg) ($p < 0.02$, ANOVA), as shown in Figure 7.

Operation of the Aeroneb Pro did not alter any of the monitored ventilator parameters. In contrast, both of the jet nebulizers increased mean airway pressure during operation by >5 cm H₂O and required adjustment of ventilator flow settings during operation to maintain ventilator parameters with initiation and discontinuation of nebulization.

Opening the medication reservoir to refill the Aeroneb Pro did not result in change of any of the ventilator parameters. In contrast, both of the jet nebulizers required interruption of ventilation in order to refill.

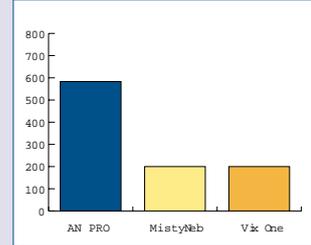


Figure 7. Amount of albuterol (µg) delivered during mechanical ventilation with HFO with each nebulizer tested.

DISCUSSION

Our findings suggest that aerosol delivery during mechanical ventilation with HFO is possible with a variety of nebulizers, although there were wide variations in delivery and impact on the ventilator settings among nebulizers. The Aeroneb Pro delivered up to three fold more drug *in vitro* than either the MistyNeb or Vix One. The gas flow required to operate both of the jet nebulizers changed ventilator parameters, while refilling the jet nebulizers required interruption of ventilation. Any changes in ventilator parameters with the Aeroneb Pro were below levels of detection.

CONCLUSION

The Aeroneb Pro delivered more albuterol during HFO to the airway of the pediatric lung model than the two small volume jet nebulizers, with no modification of ventilator parameters. This level of aerosol delivery without changes in airway pressure may make aerosol delivery during mechanical ventilation with high frequency oscillation more practical.