

In Vitro Measurement and Evaluation of Aerosol Delivery in Mechanically Ventilated Patients: Building a Database for Improved Understanding of Clinical Practice

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INTRODUCTION

Aerosol delivery to patients during mechanical ventilation is common, but methods are not standardized, and include a wide variety of techniques and devices used. Many variables¹ impact aerosol delivery during mechanical ventilation (Table 1). While *in vitro* testing has been shown to correlate to *in vivo* drug delivery,² published reports do not reflect a sufficient subset of the specific device and parameter configurations used in clinical practice throughout the world. Clinicians commonly lack the resources or expertise required to determine efficiency of aerosol delivery during mechanical ventilation. Aerogen developed and initiated a pilot program to survey the range of clinical practices and catalog the efficiencies of aerosol delivery across a variety of delivery conditions in mechanically ventilated patients.

The Aerosol Delivery Challenge™ program (ADCP) provides clinicians with access to an *in vitro* model and assay method to quantify aerosol deposition in a broad range of situations, and the ability to compare their current aerosol delivery method(s) to the Aeroneb® Professional Nebulizer System (Aeroneb Pro) in their own clinical setting.

TABLE 1: VARIABLES AFFECTING AEROSOL DELIVERY DURING MECHANICAL VENTILATION¹.

Ventilator related	Device related – MDI	Drug related
Ventilator brand used	Type of spacer/adaptor*	Dose*
Mode of ventilation*	Position in circuit*	Formulation
Tidal volume*	Timing of MDI actuation*	Aerosol particle size
Respiratory rate*		Targeted site for delivery
Duty cycle*		
Inspiratory waveform*	Aerosol Device – Neb	Patient related
Breath triggering*	Type of nebulizer used*	Severity of airway obstruction
Bias Flow*	Fill volume*	Mechanism of obstruction
	Gas flow*	Presence of dynamic hyperinflation
	Inspiration vs. continuous*	Patient-ventilator synchrony
	Duration of nebulization*	
	Position in the circuit*	
Circuit related		
Endotracheal tube*		
Inhaled gas humidity*		
Inhaled gas density*		

* variables that can be studied with the Aerosol Delivery Challenge Program.

METHODS

The ADCP provides clinical sites with an *in vitro* analysis of aerosol delivery using the specific aerosol delivery device or method, ventilators and parameters that are reflective of their current practice, and with an evaluation of the Aeroneb® Professional Nebulizer System under the same conditions. The *in vitro* model (Figure 1) allows simulation of adult, pediatric and infant ventilation and can be used with the complete range of aerosol delivery systems used in clinical practice. To reduce inconsistency in testing, trained personnel are dispatched on site to set up the model and conduct the testing. Actual testing, run in triplicate, is performed with filters collecting aerosol at the distal tip of the endotracheal tube. The filters are sent to an independent lab for blinded analysis. Specifics relating to the ventilator, circuit set-up, humidification, ventilator parameters, airway size, device used and placement are recorded on a data sheet, with copies retained by the testing site and the central study database coordinator.

METHODS (Cont'd)

The analysis includes determination of the drug quantity on each filter and % of the starting dose delivered. All results are reported to the clinical site and the database coordinator.

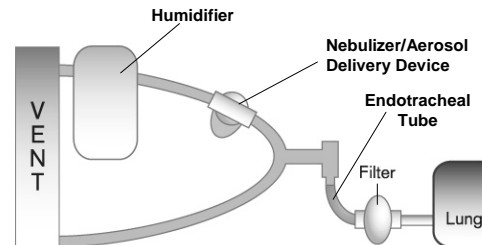


FIGURE 1: SAMPLE CIRCUIT DIAGRAM.³ PLACEMENT OF NEBULIZER OR AEROSOL DELIVERY DEVICE VARIED BASED ON HOSPITAL PRACTICE.

RESULTS AND DISCUSSION

To date, twelve Aerosol Delivery Challenge evaluations have been completed. Table 2 shows the effect of Aeroneb Pro position using three ventilator brands with a continuous bias flow ranging from 2.0 to 8.0 L/min. When the nebulizer was positioned at the wye, as the bias flow rate increased, the percent delivered decreased from 27.3% at 2.0 L/min to 4.7% and 5.2% at 3.5 L/min and 8.0 L/min, respectively. Similarly, placement of the nebulizer at the ventilator, vs. at the wye, increased delivery. During ventilation of pediatric patients (Table 3), with similar parameters, deposition ranged from 0.6% - 5.7% across a range of nebulizers. Such degrees of variance would not have been intuitive based on previously published *in vitro* work.¹⁻³

In summary, there were significant variations in aerosol delivery efficiency in different brands of ventilators set to deliver similar parameters of tidal volume, respiratory frequency and inspiratory flow. Variances in the continuous bias flow through the ventilator circuit and in nebulizer position had dramatic effects on aerosol delivery.

TABLE 2: EFFECT OF VENTILATOR TYPE, BIAS FLOW RATE, NEBULIZER POSITION, ON PERCENT OF DOSE DELIVERED *IN VITRO* USING THE AERONEB PRO WITH BASIC ADULT VENTILATION PARAMETERS.

Ventilator	Bias Flow Rate	Nebulizer Placement	% Delivered (n=3)
Siemens Servo 300A	2.0 L/min	At wye	27.3%
Siemens Servo 300A	2.0 L/min	At vent	20.8%
Puritan Bennett 840	3.5 L/min	At wye	4.7%
Puritan Bennett 840	3.5 L/min	At vent	16.2%
eVent Inspiration LS	8.0 L/min	At wye	5.2%
eVent Inspiration LS	8.0 L/min	At vent	13.4%

RESULTS AND DISCUSSION (Cont'd)

TABLE 3: TWO VENTILATORS USED TO MODEL PEDIATRIC VENTILATION USING DIFFERENT TIDAL VOLUMES, INSPIRATORY TIMES, BIAS FLOWS, NEBULIZERS AND NEBULIZER POSITIONS.

Vent Type	Volume mL	Insp. Time (s)	Bias Flow (L/min)	Nebulizer	% Delivered (n=3)	Neb Location
Servo 300	170	0.6	2	Misty Neb	0.6%	Humidifier
Servo 300	170	0.6	2	Aeroneb Pro	3.2%	Vent
Servo 300	170	0.6	2	Aeroneb Pro	3.3%	Humidifier
Servo 300	170	0.6	2	Aeroneb Pro	3.3%	Humidifier
Servo 300	170	0.6	2	Aeroneb Pro	5.7%	6" before wye
PB 840	200	0.6	3.5	WhisperJet	3.6%	6" before wye
PB 840	200	0.6	3.5	WhisperJet	3.8%	Humid + 6"
PB 840	200	0.6	3.5	Aeroneb Pro	11.7%	Humid + 6"
PB 840	200	0.6	3.5	Aeroneb Pro	14.1%	6" before wye

The ADCP was designed to avoid bias towards any single drug delivery method or device. Head to head testing of different devices was performed under identical conditions and blinded drug assays were performed at a blinded independent laboratory. As a manufacturer, it is valuable for us to understand the implications of how clinicians might use this technology. Our goal is to develop and publish a representative database cataloging current practices and relative efficiencies of aerosol delivery during mechanical ventilation.

CONCLUSION

The authors believe the ADCP will provide valuable empirical data that will assist clinicians in making informed decisions about the selection and use of aerosol technology in the treatment of mechanically ventilated patients.

REFERENCES

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