Influence of Nebulizer Type, Position, and Bias Flow on Aerosol Drug Delivery in Simulated Pediatric and Adult Lung Models During Mechanical Ventilation

Arzu Ari PhD RRT PT CPFT, Orcin Telli Atalay PhD PT, Robert Harwood MSA RRT, Meryl M Sheard MSc RRT, Essam A Aljamhan MSc RRT, and James B Fink PhD RRT FAARC

BACKGROUND: The effectiveness of aerosol drug delivery during mechanical ventilation is influenced by the patient, ventilator, and nebulizer variables. The impact of nebulizer type, position on the ventilator circuit, and bias flow on aerosol drug delivery has not been established for different age populations. OBJECTIVE: To determine the influence of nebulizer position and bias flow with a jet nebulizer and a vibrating-mesh nebulizer on aerosol drug delivery in simulated and mechanically ventilated pediatric and adult patients. METHOD: Albuterol sulfate (2.5 mg) was nebulized with a jet nebulizer and a vibrating-mesh nebulizer, using simulated pediatric and adult lung models. The 2 nebulizer positions were: (1) jet nebulizer placed 15 cm from the Y-piece adapter, and vibrating-mesh nebulizer attached directly to the Y-piece; and (2) jet nebulizer placed prior to the heated humidifier with 15 cm of large-bore tubing, and vibrating-mesh nebulizer positioned at an inlet to the humidifier. A ventilator with a heated humidifier and ventilator circuit was utilized in both lung models. The adult ventilator settings were V_T 500 mL, PEEP 5 cm H_2O, respiratory rate 20 breaths/min, peak inspiratory flow 60 L/min, and descending ramp flow waveform. The pediatric ventilator settings were V_T 100 mL, PEEP 5 cm H_2O, respiratory rate 20 breaths/min, inspiratory time 1 s. We tested bias flows of 2 and 5 L/min. The adult and pediatric lung models used 8-mm and 5-mm inner-diameter endotracheal tubes, respectively. Each experiment was run 3 times ($n = 3$). The albuterol sulfate was eluted from the filter and analyzed via spectrophotometry (276 nm). RESULTS: Nebulizer placement prior to the humidifier increased drug delivery with both the jet nebulizer and the vibrating-mesh nebulizer, with a greater increase with the vibrating-mesh nebulizer. Higher bias flow reduced drug delivery. Drug delivery with the vibrating-mesh nebulizer was 2–4-fold greater than with the jet nebulizer at all positions ($P < .05$) in both lung models. CONCLUSION: During simulated mechanical ventilation in pediatric and adult models, bias flow and nebulizer type and position impact aerosol drug delivery. *Key words: jet nebulizer; vibrating-mesh nebulizer; bias flow; nebulizer position; mechanical ventilation; drug administration; aerosol drug delivery.* [Respir Care 2010;55(7):845–851. © 2010 Daedalus Enterprises]

Introduction

Over the past few decades, aerosol drug delivery has become one of the major treatments for patients with pulmonary diseases.[1] While aerosol drug delivery is very com-

Arzu Ari PhD RRT PT CPFT, Robert Harwood MSA RRT, Meryl M Sheard MSc RRT, Essam A Aljamhan MSc RRT, and James B Fink PhD RRT FAARC are affiliated with the Division of Respiratory Therapy, School of Health Professions, Georgia State University, Atlanta, Georgia. Orcin Telli Atalay PhD PT is affiliated with the School of Physical Therapy, Pamukkale University, Denizli, Turkey.

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Correspondence: Arzu Ari PhD RRT PT CPFT, Division of Respiratory Therapy, School of Health Professions, Georgia State University, PO Box 4019, Atlanta GA 30302-4019. E-mail: aari1@gsu.edu.

mon in mechanically ventilated patients, there is an incomplete understanding of factors influencing aerosol drug deposition in intubated and mechanically ventilated patients, and the standards for aerosol delivery to different age populations are still being explored.[2,3] The efficacy of aerosol drug delivery is deeply influenced by the physical, pharmacokinetic, and pharmacodynamic properties of the drug, and by the suitability of the delivery system.[4] Previous studies indicated that several variables, such as type of aerosol generator, placement in the ventilator circuit, ventilator settings, and humidification, affect aerosol drug deposition during simulated mechanical ventilation.[3,5-17]

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Nebulizer type highly influences the efficiency of aerosol generation and aerosol drug delivery during mechanical ventilation.[3,12,13] While jet nebulizers are most commonly used, they are typically less efficient than either ultrasonic or vibrating-mesh nebulizers, which tend to have more similar aerosol drug deposition.[5,10,14] Factors such as residual drug volume, particle size, and method of generation differentiate aerosol delivery efficiency.[18] For example, the lower the residual drug volume remaining in the reservoir at end of dose, the greater the amount of drug that is emitted as aerosol. Smaller particle size is associated with less impactive aerosol loss in the ventilator circuit and airways.[3] Nebulizers that add gas flow into the ventilator circuit may dilute the aerosol and alter the delivered volumes and pressures.

Several studies have reported that the position of the aerosol generator greatly influences aerosol drug delivery in mechanically ventilated adults. For example, Hughes and Saez reported that moving the nebulizer back to the manifold position (90 cm back from the patient Y-piece) doubled the aerosol drug delivery during mechanical ventilation, compared to nebulizer placement at the Y-piece.[7] Quinn found similar improvements in aerosol delivery with a jet nebulizer placed in the inspiratory limb proximal to the ventilator rather than proximal to the patient Y-piece.[8] O'Doherty et al[9] and Thomas et al[10] compared delivery from jet and ultrasonic nebulizers placed at the Y-piece, with the addition of a 600-mL aerosol storage chamber to the ventilator circuit, and at the manifold position. The 600-mL storage chamber increased drug delivery by up to 2-fold.[9,10] More recently, Ari et al compared delivery efficiency across the range of aerosol generator types, including jet, vibrating-mesh, and ultrasonic nebulizers, and a pressurized metered-dose inhaler with chamber, at 3 positions during simulated adult mechanical ventilation, and found that the jet nebulizer provided highest efficiency when placed proximal to the ventilator.[11] They theorized that continuous gas flow from the jet nebulizer charged the inspiratory limb with aerosol between breaths, creating a functional reservoir of approximately 600 mL, similar in volume to the storage chamber used by O'Doherty et al[9] and Thomas et al.[10]

Ventilator settings such as ventilation mode, peak inspiratory flow, flow pattern, inspiratory-expiratory ratio, and V_T affect aerosol delivery and deposition during mechanical ventilation.[3,16,17] Heating and humidifying the circuit gas can reduce aerosol delivery by up to 50%, compared to ventilation under ambient conditions with anhydrous gas mixtures. To simplify the experiments, we kept these variables the same across the experiments with the adult and pediatric lung models.

Continuous bias (or trigger) flow through the ventilator circuit, to reduce patient work of breathing, is available on some ventilators. In theory, the continuous bias flow dilutes the aerosol and increases the wash-out of aerosol into the expiratory limb between breaths. Reports on aerosol from metered-dose inhaler found that bias flow had minimal impact on aerosol delivery.[19] However, the effect of various levels of bias flow on aerosol delivery with continuous nebulizers has not been well established.

A number of factors can impact the efficiency of aerosol delivery to infants and small children, compared to adults. Differences in anatomical proportion, airway size, V_T, inspiratory flow, and inspiratory-expiratory ratio reduce aerosol delivery efficiency in infants and small children.[20-23] In addition, pediatric ventilator circuit tubing has a smaller internal diameter than adult, reducing the internal volume, circuit compliance, and mechanical dead space of the ventilator circuit.[24,25] Consequently, data obtained from adult models cannot be readily extrapolated to children. In order to provide guidance to clinicians caring for critically ill patients, this study aimed to determine the influence of bias flow, nebulizer type, and position on aerosol drug delivery during simulated mechanical ventilation of pediatric and adult patients.

Methods

Design and Funding

This study was designed, performed, and analyzed at Georgia State University by and under the direct supervision of the first author, who was also the principal investigator. Aerosol devices were donated by the manufacturers, and laboratory supplies were purchased with funds from an unrestricted research grant from Aerogen, Galway, Ireland. One of the authors also serves as a scientific advisor and consultant to Aerogen. This study was initiated as part of an ongoing aerosol research program at Georgia State University and was not initiated or reviewed by any sponsor prior to its design, initiation, and analysis.

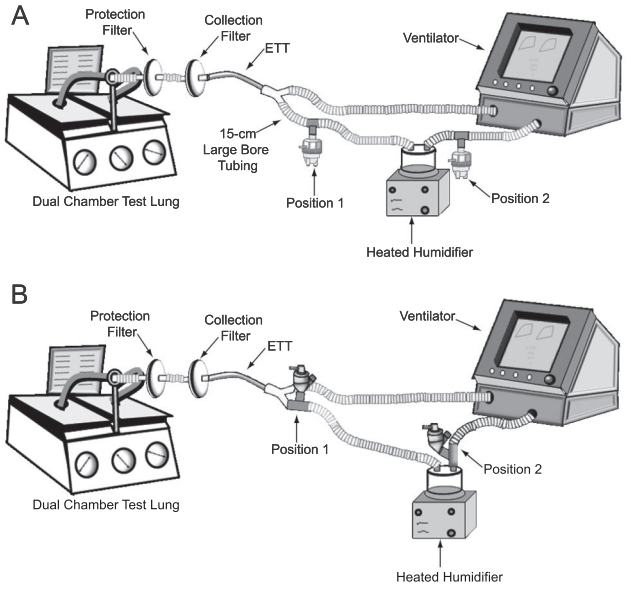

Fig. 1. Lung model of aerosol delivery with jet nebulizer (A) and vibrating-mesh nebulizer (B). The model includes a dual-chamber test lung, aerosol-collection filter, endotracheal tube, ventilator circuit, heated humidifier, and mechanical ventilator. The nebulizer circuit positions are shown.

Adult and Pediatric Lung Models

In all the experiments the model included a ventilator (Galileo, Hamilton Medical, Reno, Nevada), a heated humidifier (Fisher & Paykel, Auckland, New Zealand), a heated-wire ventilator circuit (Allegiance Healthcare, McGaw Park, Illinois) and an endotracheal tube (ETT) (Portex, Hythe Kent, United Kingdom). The ETT cuff was inflated in a 15-mm inner-diameter/22-mm outer-diameter adapter, which was then inserted into the housing of an absolute bacterial/viral filter (Respirgard II, 303, Vital Signs, Totowa, New Jersey). The tip of the ETT was 1–2 cm from the filter media. The filter was positioned superior to the distal tip of the ETT, to prevent condensate or liquid medication from reaching the filter media (Fig. 1). The natural curve of the ETT was maintained, and the filter was connected to a test lung (Michigan Instruments, Grand Rapids, Michigan) set to simulate a mechanically ventilated adult or small pediatric patient.

The pass-over humidifier and ventilator circuit were heated during ventilation for approximately 20–30 min, until the temperature at the airway was stable at 35 ± 1°C.

Ventilator Settings

To simulate adult mechanical ventilation the ventilator settings were V_T 500 mL, PEEP 5 cm H_2O, respiratory rate 20 breaths/min, peak inspiratory flow 60 L/min, descending ramp flow waveform. The adult model included a 22-mm inner-diameter, 183-cm ventilator circuit, an 8-mm inner-diameter ETT, an absolute filter, and a test lung set to a compliance of 0.1 L/cm H_2O and a resistance of 5 cm H_2O/L/s.

To simulate pediatric ventilation the ventilator settings were V_T 100 mL, PEEP 5 cm H_2O, respiratory rate 20 breaths/min, inspiratory time 1 s. The pediatric model included a 15-mm inner-diameter, 183-cm ventilator circuit, a 5-mm inner-diameter ETT, an absolute filter, and a test lung set to a compliance of 0.06 L/cm H_2O and a resistance of 8 cm H_2O/L/s. Both the adult and pediatric models were tested with bias flows of 2 and 5 L/min.

Nebulizer Type, Operation, and Doses

Two types of aerosol generators were tested:

- Jet nebulizer. We used the Misty Finity (Cardinal Health, Dublin, Ohio), which is a pneumatic Bernoulli type nebulizer. The nebulizer was attached to the ventilator circuit with a T-piece adaptor and was operated with oxygen at a flow of 2.5 L/min. The jet nebulizer uses pressurized gas to form a jet passing over a capillary tube that draws liquid formulation into the jet stream, where it is sheared from the capillary or feed tube to produce aerosol.[26,27] Baffles are used to take large particles out of suspension, returning the drug to the medication reservoir, where it can be re-nebulized. The emitted dose of the small-volume jet nebulizer may be as little as 50% of the dose placed in the nebulizer, with reported residual drug volume of 0.8–1.4 mL.[26,27] The continuous gas flow propels aerosol from the jet nebulizer into the ventilator circuit as it is generated.
- Vibrating-mesh nebulizer. We used the AeroNeb Solo (Aerogen, Mountain View, California), which uses electricity to vibrate an aperture plate (containing 1,000 funnel-shaped holes) at 128 kHz. The vibrating-mesh produces aerosol through the holes by means of a micropumping action.[28] The liquid in the reservoir is positioned above the ventilator circuit, and passes through the mesh as aerosol is generated. The emitted dose of the vibrating-mesh nebulizer can exceed 90% of the dose, with a residual drug volume of 0.1–0.3 mL. The aerosol plume from the vibrating mesh is relatively low velocity, compared to the plume from a jet nebulizer or metered-dose inhaler.

Albuterol sulfate (2.5 mg in 3 mL of normal saline) was placed in the reservoir of each nebulizer. Three of each nebulizer type/model were used for each experiment. All of the nebulizers were run continuously until they no longer produced aerosol. Each experiment was run 3 times ($n = 3$).

Table 1. Albuterol Sulfate Deposited Distal to the Endotracheal Tube

	Percent of Nominal or Emitted Dose (mean ± SD %)							
	Adult Lung Model				Pediatric Lung Model			
	Position 1		Position 2		Position 1		Position 2	
	Bias flow 2 L/min	Bias flow 5 L/min	Bias flow 2 L/min	Bias flow 5 L/min	Bias flow 2 L/min	Bias flow 5 L/min	Bias flow 2 L/min	Bias flow 5 L/min
Jet nebulizer	4.7 ± 0.1*	4.0 ± 0.1*	5.2 ± 0.2*	4.7 ± 0.4*	4.2 ± 0.2*	3.8 ± 0.3*	5.2 ± 0.3*	4.1 ± 0.4*
Vibrating-mesh nebulizer	13.4 ± 1.1	9.7 ± 0.6	23.8 ± 1.0	21.4 ± 0.4	11.4 ± 0.7	8.4 ± 0.2	13.6 ± 1.3	10.6 ± 0.3

* Significant difference between jet nebulizer and vibrating-mesh nebulizer ($p < .05$).

Nebulizer Placement

Each nebulizer was tested in 2 ventilator circuit positions:

- Position 1. The jet nebulizer was placed 15 cm from the Y-piece adapter, using standard aerosol tubing, whereas the vibrating-mesh nebulizer was attached between the Y-piece and the circuit, as suggested by the manufacturer (see Fig. 1).
- Position 2. The jet nebulizer was placed proximal to the ventilator and prior to the heated humidifier, using 15 cm of large-bore tubing to connect the nebulizer T-piece to the humidifier inlet. The vibrating-mesh nebulizer was placed with the adult 22 mm T-piece adapter at the humidifier inlet (see Fig. 1).

In Vitro Measurements

Each aerosol device was tested 3 times, at both positions, with the heated/humidified ventilator circuit (see Fig. 1). In each experiment the drug mass exiting the ETT (inhaled mass) was collected on an absolute filter at the distal tip of the ETT. On completion of each experiment, the filter was removed from the circuit, labeled, and capped. Drug was eluted with 10 mL of 0.1 molar normal hydrochloric acid, with gentle agitation for 3 min. The albuterol concentration was determined via spectrophotometry (Beckman Instruments, Fullerton, California) at a wavelength of 276 nm. The spectrophotometer was calibrated before the trials, using a holmium oxide filter (Beckman Instruments, Fullerton, California) to determine wavelength accuracy. It was then set to zero before the next trial.

Data Analysis

The amount of drug deposited on the filter was quantified and expressed as a percentage of the total drug dose placed into the nebulizer. The means and standard deviations were calculated for each component of the total inhaled drug mass. Differences in means between the inhaled mass for the 2 bias flow rates, the 2 ventilator positions, and the 2 nebulizers were compared with a 3-way factorial analysis of variance. To investigate the differences in inhaled drug mass between jet nebulizer and vibrating-mesh nebulizer at each position, a series of independent t tests were performed. Paired t tests were performed to examine the differences between the inhaled drug mass of each aerosol generator at each position and each bias flow. The differences were considered statistically significant when $P < .05$.

Results

The mean ± SD percent of the total dose of albuterol sulfate deposited on the inspiratory filter for each type of aerosol generator and position for adult and pediatric lung models and settings are shown in Table 1.

Effect of Nebulizer Type on Aerosol Drug Delivery

The mean inhaled percent of dose delivered by the vibrating-mesh nebulizer was 2–4-fold greater than that of the jet nebulizer, under all conditions, in both the adult ($P = .001$) and the pediatric ($P = .001$) lung models. Drug delivery with the jet nebulizer was similar in the adult and pediatric models, whereas delivery with the vibrating-mesh nebulizer was greater with the adult model than with the pediatric model ($P < .05$).

Effect of Nebulizer Position on Aerosol Drug Delivery

While the amount of aerosol deposition with jet nebulizer was similar at both positions in the adult and the pediatric models, the vibrating-mesh nebulizer was more efficient at position 2 with both lung models. In the adult model, placement of the vibrating-mesh nebulizer prior to the humidifier (position 2) significantly increased drug delivery at both 2 L/min ($P = .01$) and 5 L/min ($P = .001$),

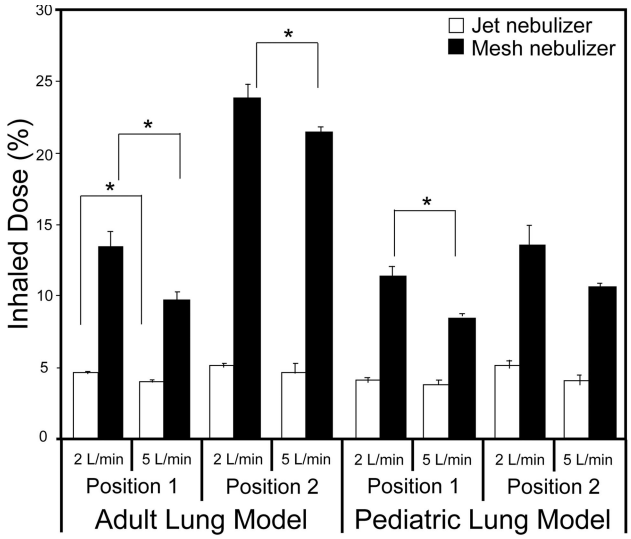

Fig. 2. Effect of position and bias flow on inhaled dose percent with a vibrating-mesh nebulizer and a jet nebulizer with adult and pediatric lung models. * Difference statistically significant.

compared to placement at the Y-piece adapter (position 1). With the pediatric model there was a trend toward greater delivery with position 2, but the increase was only significant with the vibrating-mesh nebulizer at bias flow of 5 L/min ($P = .01$) (Fig. 2).

Effect of Bias Flow on Aerosol Drug Delivery

With jet nebulizer the higher bias flow trended to reduce aerosol drug delivery in the adult and pediatric lung models at both positions, but only position 1 in the adult model was significant ($P = .006$). The vibrating-mesh nebulizer (see Fig. 2) showed significant differences between bias flow levels at position 1 ($P = .03$) and position 2 ($P = .02$) with the adult model and position 1 ($P = .01$) but not position 2 ($P = .07$) with the pediatric model.

Discussion

The present study demonstrates the influence of nebulizer type, position, and bias flow on aerosol drug delivery in models of adult and pediatric mechanical ventilation. According to the findings of this study, both position and level of bias or trigger flow impact aerosol delivery during mechanical ventilation with both adult and pediatric models.

The Effect of Nebulizer Type

The vibrating-mesh nebulizer consistently delivered more drug than the jet nebulizer, under all conditions tested. This is consistent with previous reports, and may be a function of how the aerosol is generated, the percent of dose that is emitted as aerosol, and the residual drug remaining in the nebulizer.[12,15,19,24]

The Effect of Nebulizer Position

With bias flow, the vibrating-mesh nebulizer in position 2 (proximal to the ventilator) delivered up to 2-fold more aerosol than at position 1. The impact of aerosol delivery with the jet nebulizer was less than with the vibrating-mesh nebulizer, but there was a strong trend of greater delivery with position 2.

These results are consistent with a previous study,[11] which found greater deposition from a jet nebulizer placed proximal to the ventilator (6.0 ± 0.1% of dose) compared to placement at position 1 (3.6 ± 0.2%) with an adult ventilation model with no bias flow. However, in that study the vibrating-mesh nebulizer delivered less drug when positioned at the ventilator (8.4 ± 2.1%) than near the patient Y-piece (16.7%).

The authors speculated that this effect was due in large part to the continuous gas output of the jet nebulizer, compared to the vibrating-mesh nebulizer, which generates aerosol without a secondary gas flow added to the ventilator circuit. With the jet nebulizer, during inspiration the aerosol is inhaled with the ventilator breath, but between inspirations the aerosol is driven downstream from the nebulizer. When positioned proximal to the patient, this aerosol passes into the expiratory limb. When operated at position 2, aerosol fills the inspiratory limb between the nebulizer and the patient, acting as an aerosol reservoir equivalent to the internal volume of the circuit tubing and humidifier chamber.

In contrast, aerosol generated by the vibrating-mesh nebulizer remains in the vicinity of the nebulizer until a secondary gas source, such as the ventilator breath, carries the aerosol toward the patient. When placed near the patient Y-piece (our position 1), there is a bolus of aerosol that is inhaled at the beginning of the tidal breath. When placed at the ventilator, the aerosol bolus must pass though the volume of the circuit and humidifier chamber before being inhaled. For a typical 183-cm, 22-mm inner-diameter ventilator circuit (600 mL internal volume) and heater/humidifier chamber (> 80 mL) a V_T of 500 mL would not be sufficient to carry the bolus to the patient with a single breath. The aerosol bolus would then be suspended in the inspiratory limb until delivered with the next breath, resulting in several seconds during which gravitational sedimentation would reduce the aerosol available for inspiration.

Effect of Bias Flow

Bias flow acts to move aerosol downstream. As bias flow increases, the transit time of gas (and aerosol) through

a circuit of a set volume will decrease. Our findings suggest that increasing bias flow results in a dilutive effect, with a trend toward a decrease in drug delivered, independent of the aerosol generator or position.

The internal circuit volume between the aerosol generator and the patient airway is greater with position 2. This allows the inspiratory limb to contain aerosol and act as more of a reservoir than position 1, in which aerosol is transported past the patient into the expiratory limb between inspirations.

With the vibrating-mesh nebulizer the bias flow carries aerosol downstream from the point of generation, through the inspiratory and expiratory limbs of the ventilator circuit. When placed proximal to the ventilator, position 2, in the adult circuit, the aerosol fills the inspiratory tubing, acting as a reservoir, increasing the delivered aerosol. With the smaller internal volume of the pediatric circuit, the impact of this reservoir effect is considerably less.

With the jet nebulizer the bias flow, in addition to the continuous flow from the jet nebulizer, increases the clearance rate of aerosol through the ventilator circuit. A greater reduction in delivery would be seen with jet nebulizers that utilize higher operating flows than the 2.5 L/min used in this study.

Adult Versus Pediatric Model

Aerosol delivery, with both aerosol generators, was similar at position 1 in both the adult and pediatric models. In contrast, at position 2 the deposition with the vibrating-mesh nebulizer was much higher with the adult model than with the pediatric model. This may be explained by the greater internal volume of the adult ventilator circuit and the enhanced reservoir effect described above.

Placement of the vibrating-mesh nebulizer in the pediatric circuit at position 2 resulted in similar drug delivery as position 1 in the adult circuit. With the jet nebulizer, delivery was similar at both positions across the adult and pediatric models.

Clinical Implications

While there are many findings in this study that are statistically significant (eg, effect of bias flow), the actual effect was minor and would not be expected to influence efficacy or patient safety. The findings of greatest clinical relevance are the 2–4-fold increase in drug delivery with the vibrating-mesh nebulizer, versus the jet nebulizer, in all positions, and the greater delivery in the adult circuit with the vibrating-mesh nebulizer in position 2 versus position 1. These increases in drug delivery may or may not improve bronchodilation, but may contribute to toxicity (eg, tachycardia, tremor) and may require a dose adjustment downward.

In a recent report, Moraine and co-workers found no difference in ipratropium in the urine of mechanically ventilated adult patients after 500 μg of ipratropium via nebulizer placed before the heated humidifier and at the Y-piece in the inspiratory limb.[29] This supports the premise that small statistical differences in vitro may not result in important clinical response differences, and, perhaps more importantly, that placement of the nebulizer before the heated humidifier did not reduce the amount of drug delivered and subsequently secreted in vivo.

Perhaps more important than the increase of delivered dose under some conditions are the potential benefits of nebulizer placement proximal to the ventilator, at or near the humidifier inlet. First, placement proximal to the ventilator takes the bulk and weight of the nebulizer away from the patient airway, which is of particular interest in the treatment of smaller patients.

Second, the aerosol generator is isolated from retrograde contamination of the inspiratory limb of the ventilator circuit, often introduced from the patient airway. Even should contaminated condensate enter the reservoir of the humidifier, there is no mechanism for bacteria to pass from the reservoir water to the nebulizer. It has long been established that water molecules do not offer a vehicle of transmission for bacteria.[30] In addition, there is a constant or intermittent flow of gas downstream, away from the nebulizer.

Third, a large proportion of rain-out from the aerosol generator deposits in the humidifier rather than in the circuit, reducing the liquid condensate load. This reduces the risk of nebulizers with lower residual volume of depositing greater volumes of liquid in the inspiratory limb, reducing the risk of occlusion of the airway by condensate.

This raises a concern of the effect of heating the medication in the heated humidifier reservoir for an extended period. While most drugs have been studied for stability up to 40°C, few are studied at the $\geq$ 70°C that may exist in the heater reservoir for periods of a week or more. Additional research should be performed to determine the impact on drug integrity and the production of hazardous vapors under such conditions.

Limitations

While the results of this study provide insights into the effect of placement of 2 types of aerosol generator in the ventilator circuit and the impact of bias flow, results may vary with different nebulizers commonly used in clinical practice. For example, the jet nebulizer used in this study required an operating flow of 2.5 L/m, whereas other jet nebulizers utilize flows as high as 10 L/min, which may further reduce aerosol transit time through the circuit, reducing aerosol drug delivery. Similarly, the ventilator settings tested, while representative of adult and pediatric

settings, do not speak to the broad array of settings and ventilation modes used in clinical practice.

Common to other in vitro models that have collected drug on an absolute filter, the deposited dose does not reflect the amount of inhaled aerosol that would be exhaled in vivo (typically a small percentage of what is inhaled), consequently underestimating the in vitro dose. However, this in vitro model does provide perspective on the inhaled dose as compared across the variables tested.

Future Research

Additional studies with a broader range of devices and settings would help to provide additional guidance to clinicians in evaluating their ability to optimize aerosol delivery with both adult and pediatric patients.

Conclusions

In conclusion, aerosol delivery depends on the nebulizer type, position, and bias flow during simulated adult and pediatric mechanical ventilation. With bias flow, placement of the vibrating-mesh nebulizer and jet nebulizer prior to the humidifier delivered more aerosol than placement at the Y-piece. Higher bias flow decreased aerosol drug delivery in our models of adult and pediatric mechanical ventilation. A better understanding of these factors and their effects on aerosol delivery can help to guide clinicians to increase the efficiency of aerosol therapy administered to mechanically ventilated patients.

REFERENCES

1. Terzano C, Allegra L. Importance of drug delivery system in steroid aerosol therapy via nebulizer. Pulm Pharmacol Ther 2002;15(5):449-454.
2. Dhand R. Aerosol therapy during mechanical ventilation: getting ready for prime time. Am J Respir Crit Care Med 2003;168(10):1148-1149.
3. Miller DD, Amin MM, Palmer LB, Shah AR, Smaldone GC. Aerosol delivery and modern mechanical ventilation: in vitro/in vivo evaluation. Am J Respir Crit Care Med 2003;168(10):1205-1209.
4. Kendrick A, Smith E, Wilson R. Selecting and using nebulizer equipment. Thorax 1997;52(Suppl 2):92-101.
5. Pedersen K, Handlos V, Heslet L, Kristensen H. Factors influencing the in vitro deposition of tobramycin aerosol: a comparison of an ultrasonic nebulizer and a high frequency vibrating mesh nebulizer. J Aerosol Med 2006;19(2):175-183.
6. McPeck M, Tandon R, Hughes K, Smaldone GC. Aerosol delivery during continuous nebulization. Chest 1997;111(5):1200-1205.
7. Hughes J, Saez J. Effectsof nebulizer mode and position in a mechanical ventilator circuit on dose efficiency. Respir Care 1987;32(12):1131-1135.
8. Quinn W. Effect of a new nebulizer position on aerosol delivery during mechanical ventilation. Respir Care 1992;37(5):423-431.
9. O'Doherty MJ, Thomas SH, Page CJ, Treacher DF, Nunan TO. Delivery of a nebulized aerosol to a lung model during mechanical ventilation: effect of ventilator settings and nebulizer type, position, and volume of fill. Am Rev Respir Dis 1992;146(2):383-388.
10. Thomas SH, O'Doherty MJ, Page CJ, Treacher DF, Nunan TO. Delivery of ultrasonic nebulized aerosols to a lung model during mechanical ventilation. Am Rev Respir Dis 1993;148(4):872-877.
11. Ari A, Areabi H, Sampson J. Evaluation of position of aerosol device in two different ventilator circuits during mechanical ventilation (abstract). Respir Care 2007;52(11):1580.
12. Hess D, Fisher D, Williams P, Pooler S, Kacmarek RM. Medication nebulizer performance. Effects of diluent volume, nebulizer flow, and nebulizer brand. Chest 1996;110(2):498-505.
13. O'Riordan TG, Greco MJ, Perry RJ, Smaldone GC. Nebulizer function during mechanical ventilation. Am Rev Respir Dis 1992;145(5):1117-1122.
14. Di Paolo ER, Pannatier A, Cotting J. In vitro evaluation of bronchodilator drug delivery by jet nebulization during pediatric mechanical ventilation. Pediatr Crit Care Med 2005;6(4):462-469.
15. Zhang G, David A, Wiedmann TS. Performance of the vibrating membrane aerosol generation device: Aeroneb Micropump nebulizer. J Aerosol Med 2007;20(4):408-416.
16. Thomas SH, O'Doherty MJ, Fidler HM, Page CJ, Treacher DF, Nunan TO. Pulmonary deposition of a nebulised aerosol during mechanical ventilation. Thorax 1993;48(2):154-159.
17. Dolovich MA. Influence of inspiratory flow rate, particle size, and airway caliber on aerosolized drug delivery to the lung. Respir Care 2000;45(6):597-608.
18. Ari A, Hess D, Myers T, Rau JL. A guide to aerosol delivery devices for respiratory therapists. Dallas, Texas: American Association for Respiratory Care; 2009.
19. Fink JB, Dhand R, Grychowski J, Fahey PJ, Tobin MJ. Reconciling in vitro and in vivo measurements of aerosol delivery from a metered-dose inhaler during mechanical ventilation and defining efficiency-enhancing factors. Am J Respir Crit Care Med 1999;159(1):63-68.
20. Everard ML. Inhalation therapy for infants. Adv Drug Deliv Rev 2003;55(7):869-878.
21. Everard ML. Inhaler devices in infants and children: challenges and solutions. J Aerosol Med 2004;17(2):186-195.
22. Everard ML. Aerosol delivery to children. Pediatr Ann 2006;35(9):630-636.
23. Ahrens RC. The role of the MDI and DPI in pediatric patients: "children are not just miniature adults". Respir Care 2005;50(10):1323-1328.
24. Bisgaard H. Delivery of inhaled medication to children. J Asthma 1997;34(6):443-467.
25. Fink J. Aerosol delivery to ventilated infants and pediatric patients. Respir Care 2004;49(6):653-665.
26. Fink JB. Humidity and aerosol therapy. In: Mosby's Respiratory Care Equipment. St Louis: Mosby-Elsevier; 2010:91-140.
27. Fink JB. Aerosol drug therapy. In: Egan's Fundamentals of Respiratory Care, 9th edition. St Louis: Mosby Elsevier; 2009:801-842.
28. Dhand R. Nebulizers that use a vibrating mesh or plate with multiple apertures to generate aerosol. Respir Care 2002;47(12):1406-1416.
29. Moraine J, Truflandier K, Vandenbergen N, Berre J, Melot C, Vincent J. Placement of the nebulizer before the humidifier during mechanical ventilation: effect on aerosol delivery. Heart Lung 2009;38(5):435-439.
30. Rhame F, Streifel A, McComb C. Bubbling humidifiers produce microaerosols which can carry bacteria. Infection Control 1986;7(8):403-407.