

Albuterol Delivery via Tracheostomy Tube

Christopher M Piccuito RRT and Dean R Hess PhD RRT FAARC

HYPOTHESIS: Albuterol delivery through a tracheostomy tube is affected by device (nebulizer vs metered-dose inhaler), interface (mask vs T-piece), bias flow, and humidification. **METHODS:** A lift bar was placed between the chambers of a dual-chambered lung model such that a ventilator triggered simulated spontaneous breathing at a rate of 20 breaths/min, tidal volume of 0.4 L, and inspiratory-expiratory ratio of 1:2. An 8-mm inner diameter cuffed tracheostomy tube was placed through a semi-circular model that simulated a patient's neck. Four conditions of gas flow and humidification were used for the nebulizer experiments: heated aerosol (approximately 30 L/min, approximately 30°C), heated humidity (approximately 30 L/min, approximately 30°C), high flow without added humidity (approximately 30 L/min), or a nebulizer attached to the tracheostomy tube without additional flow. The nebulizer was filled with 4 mL that contained 2.5 mg of albuterol, and operated at 8 L/min. The nebulizer was tested with a T-piece or tracheostomy mask. For the metered-dose inhaler experiments, a spacer was used and actuation of the inhaler (100 µg per actuation) was synchronized with inhalation (4 actuations separated by ≥ 15 s). When the spacer was used without additional flow, a valved T-piece was used with a 1-way valve placed either proximal or distal to the spacer. A filter was attached between the lung model and the distal end of the tracheostomy tube. Albuterol washed from the filter was measured by ultraviolet spectrophotometry. **RESULTS:** For the nebulizer, the most efficient delivery was with no flow other than that to power the nebulizer and with a T-piece ($p < 0.001$). The most efficient method for aerosol delivery was metered-dose inhaler with a valved T-piece and placement of the 1-way valve in the proximal position ($p < 0.001$). The effect of humidity was unclear from the results of this study. **CONCLUSIONS:** Albuterol delivery via tracheostomy was affected by the delivery device (nebulizer vs inhaler), bias gas flow, and the patient interface. *Key words: aerosol, bronchodilator, metered-dose inhaler, nebulizer, tracheostomy.* [Respir Care 2005;50(8):1071–1076. © 2005 Daedalus Enterprises]

Introduction

Inhaled albuterol is occasionally used in spontaneously breathing patients with a tracheostomy tube. Al-

though much has been published about aerosol delivery through endotracheal tubes (ETTs) in mechanically ventilated patients,^{1–6} there has been surprisingly little published about delivery through tracheostomy tubes in spontaneously breathing patients. A thorough literature search uncovered only a few case reports of methods used to adapt metered-dose inhalers (MDIs) to tracheostomies in ambulatory patients.^{7–9}

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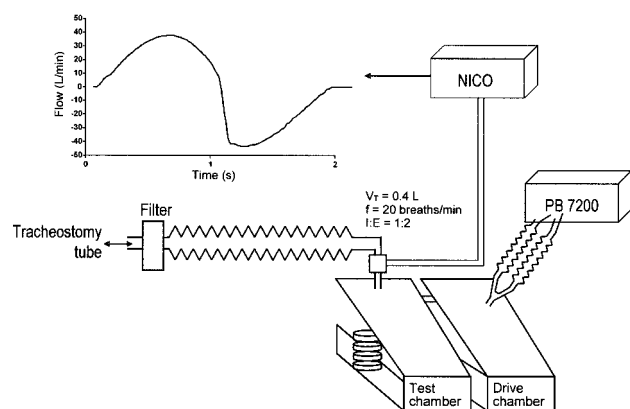


Fig. 1. Schematic representation of the experimental setup. Also shown is the actual flow pattern recorded from the NICO monitor. V_T = tidal volume. f = respiratory frequency. I:E = inspiratory-expiratory ratio. PB = Puritan-Bennett.

MacIntyre¹ identified 4 important factors in optimizing delivery through an artificial airway: ventilation pattern and timing of aerosol delivery, carrier gas properties, the nebulizing device, and circuit properties. Aerosol delivery is improved with a slow inspiratory flow and large tidal volume, timing of aerosol delivery to the inspiratory phase, a dry carrier gas, an efficient nebulizer, and a holding chamber with MDI use. Virtually all studies of these factors have been with an ETT and positive-pressure ventilation. O'Riordan et al¹⁰ studied aerosol deposition in mechanically ventilated patients with tracheostomies. They reported that the tracheostomy tube was not an important barrier to lung deposition, with < 3% of the aerosol depositing on the tracheostomy tube. Using in vitro and in vivo models of aerosol delivery during mechanical ventilation, in which 3 of 6 patients had tracheostomies, Miller et al¹¹ reported that breath-actuated nebulization and humidity were the most important factors in aerosol delivery.

In the acute-care setting, patients with tracheostomy typically have a high flow of humidified oxygen delivered to the tracheostomy tube. We have observed a variety of methods to deliver inhaled bronchodilators via nebulizer or MDI to these patients. We have heard conflicting biases regarding this practice and felt it important to conduct this in vitro study to provide guidance for the best approach to this therapy. Our hypothesis was that albuterol delivery through a tracheostomy tube is affected by type of aerosol delivery (nebulizer vs MDI), patient interface (mask vs T-piece), bias flow, and humidification of the inspired gas.

Methods

Experimental Model

A Puritan-Bennett 7200 ventilator (Puritan-Bennett, Carlsbad, California) was attached to one chamber of a

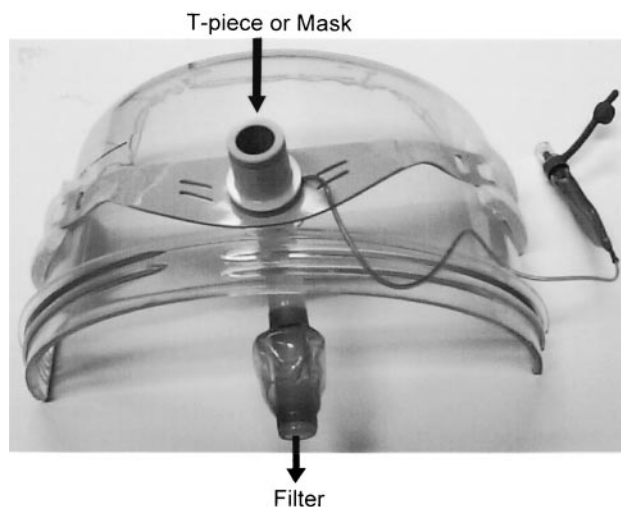


Fig. 2. The semi-circular model, which simulated a patient's neck.

dual-chamber test lung (Michigan Instruments, Grand Rapids, Michigan) (Fig. 1). A lift bar was placed between the chambers, such that the ventilator simulated spontaneous breathing of the second chamber at a rate of 20 breaths/min, tidal volume of 0.4 L, inspiratory-expiratory ratio of 1:2, and quasi-sinusoidal inspiratory flow pattern (measured with a Novamatrix NICO, Respironics, Murrysville, Pennsylvania). An 8-mm inner diameter cuffed tracheostomy tube (Portex Blue Line, Smiths Medical, Keene, New Hampshire) was placed through a semi-circular model that simulated a patient's neck (Fig. 2). A Puritan-Bennett D/Flex filter was attached between the lung model and the distal end of the tracheostomy tube to capture aerosol delivered through the tracheostomy tube.

Nebulizer Testing Conditions

A Hudson MicroMist nebulizer (Hudson, Temecula, California) was filled with 4 mL that contained 2.5 mg of albuterol, and operated at 8 L/min, using a calibrated flow meter (Timemeter 0-15, St Louis, Missouri). The MicroMist nebulizer emits an aerosol with a mass median aerodynamic diameter of 2.4 μm , and 70% of the particles have a size < 4.7 μm . The nebulizer was tested with a T-piece/flex tube or tracheostomy mask (Hudson RCI, Temecula, California) inserted about 15 cm from the interface (Fig. 3). Four conditions ($n = 5$ each) of gas flow and humidification were used for the nebulizer experiments:

1. Heated aerosol. Heated aerosol was generated using a Baxter nebulizer cap and heater (Baxter Healthcare, Deerfield, Illinois). The nebulizer was powered with an oxygen flow of 8 L/min (Timemeter 0-15, St Louis, Missouri) and an oxygen concentration setting of 40%, to produce an outlet flow of approximately 30 L/min. Gas temperature measured at the proximal tracheostomy tube was approx-

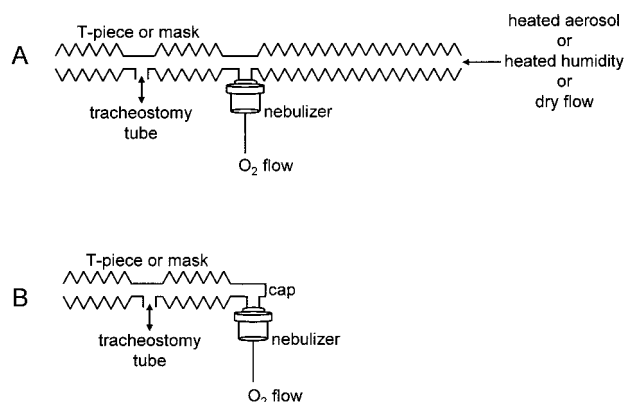


Fig. 3. Schematic representation of the setup used for the nebulizer experiments. A: High-flow setup. B: Setup using a nebulizer without additional flow.

imately 30°C (traceable double thermometer, Control Company, Friendswood, Texas) and relative humidity was > 95% (digital hygrometer, Fisher Scientific, Hampton, New Hampshire).

2. Heated humidity. A Concha-Therm heated humidifier (Hudson RCI, Temecula, California) was used to generate high-flow heated humidity. A calibrated flow meter (Time-meter 0–75, St Louis, Missouri) was set to deliver an oxygen flow of approximately 30 L/min. The heat of the humidifier was adjusted to produce a gas temperature at the proximal airway of approximately 30°C with a relative humidity > 95%.

3. High flow without added humidity. A calibrated flow meter was set to deliver an oxygen flow of approximately 30 L/min. Relative humidity was < 5%.

4. Nebulizer attached to the tracheostomy tube without additional gas flow. No additional flow was added other than that generated by the medication nebulizer. One side of the T-piece attached to the nebulizer was capped. The other side of the T-piece was attached to the 15-cm flexible tube leading to the T-piece or tracheostomy mask connected to the tracheostomy tube.

MDI Testing Conditions

For the MDI experiments, a Monaghan AeroVent spacer (Monaghan, Plattsburgh, New York) was used, and actuation of a pressurized MDI (100 µg of albuterol from the valve per actuation) (albuterol inhalation aerosol, Warrick Pharmaceuticals, Reno, Nevada) was synchronized with inhalation (4 actuations, separated by ≥ 15 s). Four conditions (*n* = 5 each) of gas flow and humidity were used with the MDI experiments (Fig. 4):

1. Heated humidity with T-piece. A Concha-Therm heated humidifier was used to generate high-flow heated humidity (approximately 30 L/min). The humidifier was

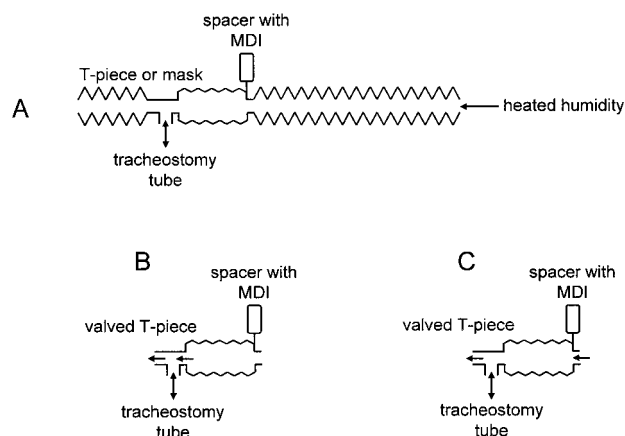


Fig. 4. Schematic representation of the experimental setup used for the metered-dose inhaler (MDI) experiments. A: Setup with spacer in-line, with high flow. B: Setup using valved T-piece with valve distal to spacer. C: Setup using valved T-piece with valve proximal to spacer.

adjusted to produce a gas temperature at the proximal airway of approximately 30°C and a relative humidity > 95%. The patient connection was a T-piece.

2. Heated humidity with tracheostomy mask. A Concha-Therm heated humidifier was used to generate high-flow heated humidity (approximately 30 L/min). The humidifier was adjusted to produce a gas temperature at the proximal airway of approximately 30°C and relative humidity > 95%. The patient connection was a tracheostomy mask.

3. AeroVent with valved T-adapter. No additional flow was added other than that generated by the simulated spontaneous breathing. The standard open T-piece at the proximal tracheostomy tube was replaced with a valved T-adapter (Airlife ventilator monitoring adapter, Allegiance Healthcare, McGaw Park, Illinois). With this configuration the patient inhales from the spacer but exhales away from the spacer.

4. AeroVent with valved T-adapter and 1-way valve proximal to AeroVent. No additional flow was added other than that generated by the simulated spontaneous breathing. The standard open T-piece at the proximal tracheostomy tube was replaced with a valved T-adapter, but the valve between the AeroVent and T-piece was moved to a position at the proximal opening to the AeroVent.

Albuterol Measurement

For the nebulizer experiments, 20 mL of 0.9% saline solution was used to wash the aerosol collected on the filter. The filter was shaken for 1 min to ensure proper mixing. The light absorption of the solution washed from the filter was measured with a spectrophotometer (DU Series 500, Beckman Instruments, Fullerton, California)

using a 1-mL quartz cuvette, at a wavelength of 276 nm. The amount of albuterol captured on the filter was calculated from the absorption-concentration standard curve generated by plotting light absorption as a function of albuterol concentration. There was a linear relationship between absorption and concentration of albuterol between 0 and 0.05 mg/mL, with a slope of 0.1426 ($r^2 = 0.99$). For the MDI experiments, the filter was washed with 0.1 M NaOH and analyzed at 243 nm. The standard curve for these experiments was linear between 0 $\mu\text{g/mL}$ and 100 $\mu\text{g/mL}$, with a slope of 0.0323 ($r^2 = 0.99$). Our methodology for the assay of albuterol was adapted from that reported in the literature.^{12,13} We have commonly used this assay in our laboratory to measure albuterol output from nebulizers and MDIs. Accordingly, we used methodology in this study with which we were most confident.

We tested the ability of the filters to trap aerosol by placing 2 filters in series and found that there was no albuterol detected in the second filter. We also tested the specificity of our analytic technique by nebulization of saline, for which we found that there was no absorption. A known amount of albuterol was mixed in the filter with saline to determine whether all albuterol was recovered, and we found that all albuterol was detected when the filter was shaken for at least 1 min.

Statistical Analysis

The amount of albuterol delivered was expressed in absolute terms and as a percentage of the nominal dose. The nominal dose for the nebulizer was the dose placed into the nebulizer cup (2.5 mg), and the nominal dose for the MDI was 400 μg (4 puffs, 100 $\mu\text{g/puff}$). Summary data are reported as mean \pm standard deviation. Comparisons between groups were analyzed using univariate analysis of variance. Post-hoc comparisons were made with Scheffé analysis. All statistical analysis was performed using commercially available software (SPSS version 11.5, SPSS, Chicago, Illinois). Differences were considered statistically significant when $p < 0.05$.

Results

Nebulizer Studies

For the nebulizer studies (Fig. 5 and Table 1), the most efficient delivery was with no flow other than that to power the nebulizer ($p < 0.001$ via Scheffé post-hoc analysis, compared to the other treatment conditions). The delivered dose was greater with a T-piece than with the tracheostomy mask ($p = 0.001$), with no significant interaction effect between the treatment conditions and the type of interface ($p = 0.22$).

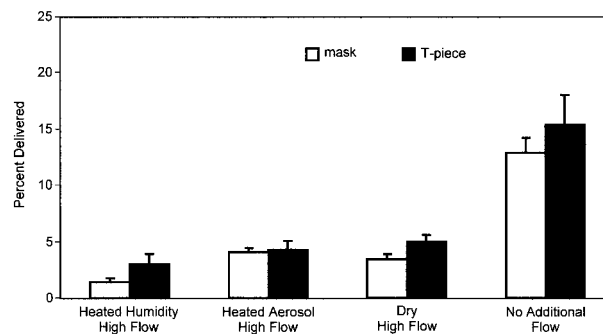


Fig. 5. Percent of the nominal dose of albuterol delivered via nebulizer, using the 4 delivery methods described in the text. Note that the most efficient delivery was with no flow other than that to power the nebulizer and a T-piece ($p < 0.001$). The delivered dose was greater with a T-piece than with the tracheostomy mask ($p = 0.001$).

Table 1. Albuterol Delivered Via Various Nebulizer Methods*

Method	Absolute Amount (μg)	Percent
Heated Aerosol		
Mask	103.2 \pm 7.5	4.1 \pm 0.3
T-piece	107.0 \pm 19.8	4.3 \pm 0.8
Heated Humidity		
Mask	36.2 \pm 7.8	1.4 \pm 0.3
T-piece	75.2 \pm 21.7	3.0 \pm 0.9
Dry High		
Mask	86.6 \pm 10.3	3.5 \pm 0.4
T-piece	124.8 \pm 15.3	5.0 \pm 0.6
Nebulizer to Tracheostomy Tube		
Without Additional Flow		
Mask	322.0 \pm 32.8	12.9 \pm 1.3
T-piece	382.0 \pm 67.9	15.3 \pm 2.7

*Values are mean \pm SD

MDI Studies

The most efficient method for aerosol delivery was via MDI with valved T-piece and placement of the 1-way valve in the proximal position ($p < 0.001$) (Fig. 6 and Table 2). This method delivered a significantly greater dose than each of the other methods ($p < 0.001$ via Scheffé post-hoc analysis).

Nebulizer Versus MDI Comparisons

Comparing nebulizer and MDI using a T-piece and high-flow heated humidity, there was no significant difference in the absolute amount of albuterol delivery ($p = 0.30$). However, the efficiency of the MDI was greater than that of the nebulizer, with a significantly greater percentage of

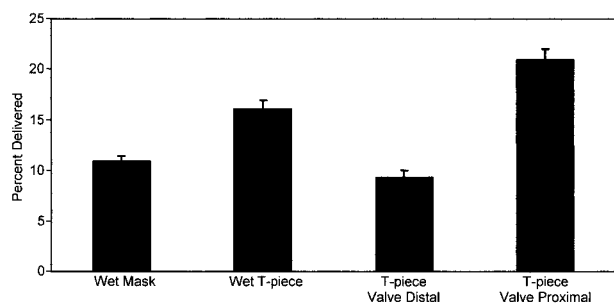


Fig. 6. Percent of the nominal dose of albuterol delivered via the 4 delivery methods described in the text. The most efficient method for aerosol delivery was via metered-dose inhaler with valved T-piece and placement of the 1-way valve in the proximal position ($p < 0.001$).

Table 2. Albuterol Delivered Via Various Metered-Dose-Inhaler Methods*

Method	Absolute Amount (μg)	Percent
Heated humidity, T-piece	64.4 ± 3.7	16.1 ± 0.9
Heated humidity, tracheostomy mask	43.7 ± 2.2	10.9 ± 0.6
No additional flow, valve distal	37.1 ± 3.0	9.3 ± 0.7
No additional flow, valve proximal	83.8 ± 4.2	20.9 ± 1.0

*Values are mean \pm SD

the nominal dose delivered via MDI ($p < 0.001$). When using a tracheostomy mask rather than the T-piece, again there was no significant difference in the absolute amount of albuterol delivery ($p = 0.07$), but the MDI was more efficient in relation to the percentage of the nominal dose delivered ($p < 0.001$). When comparing the most efficient nebulizer technique (T-piece, no additional flow) to the most efficient MDI technique (valved T-piece with valve proximal to holding chamber), the nebulizer delivered a much larger dose in absolute terms ($382 \pm 68 \mu\text{g}$ vs $84 \pm 4 \mu\text{g}$, $p < 0.001$), but the efficiency of delivery was greater for the MDI than the nebulizer ($21 \pm 1\%$ vs $15 \pm 3\%$, $p = 0.002$).

Humidity

For the nebulizer experiments, albuterol delivery was greater for the high-flow dry gas than high flow with humidified gas ($p = 0.007$). Albuterol delivery was also greater for the heated aerosol group than the humidified high-flow group ($p = 0.008$). There was no significant difference in albuterol delivery for the high flow with dry gas, compared to the heated aerosol group ($p = 1.0$).

Discussion

The major findings of this study are: (1) a measurable amount of albuterol aerosol was delivered through the tracheostomy tube in this model of spontaneous breathing, whether a nebulizer or MDI with spacer was used; (2) delivery of albuterol aerosol into a high gas flow was inefficient for the nebulizer; (3) use of a T-piece resulted in more albuterol delivery than use of a tracheostomy mask; (4) efficiency was greater for the MDI with valved holding chamber than for the nebulizer; (5) the MDI was most efficient when a valved T-piece was used and the valve was placed proximal rather than distal to the spacer; and (6) the effect of humidity on albuterol delivery is not clear.

The amount of aerosol delivered to a filter at the distal ETT during mechanical ventilation has been reported as low as 1% and as high as 40%, depending upon a variety of measurement conditions.¹ For the conditions we studied, the amount of albuterol delivered to the distal tracheostomy tube varied from about 1% to about 20%. Thus it might be argued that the delivery of albuterol during spontaneous breathing through a tracheostomy tube is roughly comparable to delivery of albuterol through an ETT during mechanical ventilation. We did not evaluate the delivery of albuterol through an ETT during spontaneous breathing. We would speculate, however, that if all other factors are kept constant, aerosol delivery through a tracheostomy tube would be greater than through an ETT, because of the shorter length of the tracheostomy tube. The purpose of our study was not to compare aerosol delivery through a tracheostomy tube compared to an ETT, but rather to compare methods of albuterol delivery with a tracheostomy tube. O'Riordan et al¹⁰ reported that the tracheostomy tube was not an important barrier to delivery of aerosol into the lower respiratory tract.

In the nebulizer experiments, we found that the amount of albuterol delivered to the distal tracheostomy tube was significantly reduced when the nebulizer was attached in-line with a high-flow oxygen-delivery device. This is presumably the result of aerosol waste to the ambient air. Our results suggest that a nebulizer without additional gas flow and a T-piece should be used in spontaneously breathing patients with tracheostomies. This results in a 3-fold or greater delivery of albuterol. These data are supported by the study by Parkes and Bersten,⁹ who compared aerosol delivery with a conventional face mask versus a high-flow system with continuous positive airway pressure. When a nebulizer was placed into a high flow of 50 L/min, they reported that the amount of study drug deposited in the lower respiratory tract decreased from about 7% to about 1%. We were not surprised that more aerosol was delivered with the T-piece than with the tracheostomy mask. The T-piece directs the aerosol to the proximal tracheos-

tomy tube, whereas the tracheostomy mask results in more waste of drug to the ambient air.

Our data suggest that an MDI can be used to deliver albuterol through a tracheostomy tube during spontaneous breathing. The efficiency of the MDI was higher than that of the nebulizer. However, our data also suggest that a valved T-piece should be used, and moreover, the valve should be placed proximal to the spacer rather than distal to the spacer. Moving the valve from a distal to a proximal position resulted in a nearly 2-fold increase in albuterol delivery. Presumably, placement of the valve distal to the spacer results in impaction of aerosol on the valve and reduced aerosol delivery from the spacer. It is also important to note that, although the efficiency of the MDI is greater than the nebulizer, the absolute dose is greater with the nebulizer when used in its most efficient configuration because of the much greater nominal dose placed into the nebulizer cup. Thus, the nebulizer might be superior to the MDI if a large dose is required. Alternatively, a greater number of actuations can be delivered from the MDI.

The influence of humidity on albuterol delivery is not clear in our study. With the high-flow setup, more albuterol was delivered with dry gas than with humidified gas. This is consistent with the results of studies that have evaluated the effect of humidity on aerosol delivery during mechanical ventilation.^{11,14,15} The absence of an effect of heated aerosol on albuterol delivery, compared to dry high flow, was a surprise finding for which we have no explanation. It is of interest to note that none of the studies of the influence of humidity on albuterol delivery during mechanical ventilation used a heated aerosol.

Several papers have described modifications of MDI spacers to allow attaching the spacer to a tracheostomy tube.^{7,8} In one patient, use of a spacer with albuterol MDI adapted to a tracheal stoma was reported to produce an increase in peak expiratory flow and forced expiratory volume in the first second.⁷ In another case, minor hemoptysis and extensive granulation tissue on the carina-adjacent bronchi was reported, because of frequent spraying of an MDI directly into a permanent tracheostomy.¹⁶ In that case, the hemoptysis and pathologic changes resolved with the addition of a spacer adapted to fit the tracheal stoma.

Limitations

Because this was a bench study, the results should be subjected to clinical validation. Moreover, we studied only one nebulizer brand, one ventilatory pattern, one type of tracheostomy tube, and one brand of MDI spacer. Consistent with our hypothesis, we limited variables such as tracheostomy tube size, breathing pattern, and nebulizer type to focus on our primary study objectives. Future work

should address the roles of these variables on aerosol delivery through a tracheostomy tube. Despite these limitations, we believe that this study provides clinically useful insights into aerosol delivery for spontaneously breathing patients with tracheostomies.

Conclusions

Albuterol delivery using an MDI and valved holding chamber was more efficient than a small-volume nebulizer. Bias flow using a nebulizer led to a decrease in albuterol delivery. The findings regarding the impact of humidity on aerosol delivery are not clear.

REFERENCES

- MacIntyre NR. Aerosol delivery through an artificial airway. *Respir Care* 2002;47(11):1279–1285.
- Dhand R. Basic techniques for aerosol delivery during mechanical ventilation. *Respir Care* 2004;49(6):611–622.
- Dhand R. Special problems in aerosol delivery: artificial airways. *Respir Care* 2000;45(6):636–645.
- Duarte AG, Fink JB, Dhand R. Inhalation therapy during mechanical ventilation. *Respir Care Clin N Am* 2001;7(2):233–260.
- Dhand R, Tobin MJ. Inhaled bronchodilator therapy in mechanically ventilated patients. *Am J Respir Crit Care Med* 1997;156(1):3–10.
- Dhand R, Tobin MJ. Bronchodilator delivery with metered-dose inhalers in mechanically-ventilated patients. *Eur Respir J* 1996;9(3):585–595.
- Mirza S, Hopkinson L, Malik TH, Willatt DJ. The use of inhalers in patients with tracheal stomas or tracheostomy tubes. *J Laryngol Otol* 1999;113(8):762–764.
- Nakhla V. A homemade modification of a spacer device for delivery of bronchodilator or steroid therapy in patients with tracheostomies. *J Laryngol Otol* 1997;111(4):363–365.
- Parkes SN, Bersten AD. Aerosol kinetics and bronchodilator efficacy during continuous positive airway pressure delivered by face mask. *Thorax* 1997;52(2):171–175.
- O’Riordan TG, Palmer LB, Smaldone GC. Aerosol deposition in mechanically ventilated patients: optimizing nebulizer delivery. *Am J Respir Crit Care Med* 1994;149(1):214–219.
- 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.
- 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.
- Fink JB, Dhand R, Grychowksi 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.
- Fink JB, Dhand R, Duarte AG, Jenne JW, Tobin MJ. Aerosol delivery from a metered-dose inhaler during mechanical ventilation: an in vitro model. *Am J Respir Crit Care Med* 1996;154(2 Pt 1):382–387.
- Diot P, Morra L, Smaldone GC. Albuterol delivery in a model of mechanical ventilation: comparison of metered-dose inhaler and nebulizer efficiency. *Am J Respir Crit Care Med* 1995;152(4 Pt 1):1391–1394.
- Newhouse MT. Hemoptysis due to MDI therapy in a patient with permanent tracheostomy: treatment with mask AeroChamber. *Chest* 1999;115(1):279–282.