Comparison of Aerosol Delivery During Simulated Adult Noninvasive Positive Pressure Ventilation: Nebulizer versus Pressurized Metered-dose Inhaler

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ABSTRACT

Objective: To elucidate the factors influencing aerosol delivery to the lower respiratory tract during noninvasive ventilation.

Experimental Design: The rapid and shallow breathing of an adult patient receiving noninvasive ventilation (S/T mode, non-humidified circuit, RR 20 breaths/min, I:E ratio 1:2, V_T 300 ml, airway resistance 20 cmH_2O/L/s and compliance 0.07 L/cmH_2O, and inspiratory/ expiratory positive airway pressure (IPAP/EPAP) of 10/5, 15/5 or 15/10 cm H_2O, respectively) was mimicked *in vitro*. Albuterol sulfate aerosols were administered via a pressurized metered-dose inhaler (pMDI) with spacer chamber, a vibrating aperture plate (VAP) and a jet nebulizer, placed sequentially at proximal, in-between and distal positions in-line in the circuit. Three experiments were performed for each of the 3 aerosol devices, at each of the 3 positions and under each of 3 pressure support settings. Drug was eluted from a filter placed at the distal ends of the bronchi and quantified by a spectrophotometer (276 nm) after each experiment.

Results: The efficiency of aerosol delivery varied significantly, depending on the type of aerosol device and its position in the circuit. Aerosol generators placed at the distal position showed the highest efficiency compared to at in-between or proximal position (P<0.001). In general, VAP nebulizer was more efficient than jet nebulizer and pMDI (6.1±2.9% vs. 3.68±1.06% and 1.05±0.73%, F=111.92, P<0.001). In addition, the pressure support settings had lesser effect on efficiency of aerosol delivery.

Conclusions: During noninvasive ventilation, aerosol delivery with different aerosol generators showed significant variability. A VAP nebulizer placed distal to the air leak in the circuit had a higher efficiency than a jet nebulizer or pMDI. The efficiency of aerosol delivery with a pMDI would need to be significantly enhanced for this delivery method to be practical for clinical use during noninvasive ventilation.

INTRODUCTION

Delivery of bronchodilator drugs via aerosol generators during noninvasive ventilation (NIV) is the preferred method for management of patients with worsening COPD and acute asthma.

There is limited information about the influence of the type of aerosol device and its position in the circuit, inhaled gas humidity, pressure support settings of the ventilator and patient related factors on aerosol delivery to the lower respiratory tract during NIV.

We hypothesized that efficiency of aerosol delivery to the lower respiratory tract via aerosol generators during NIV would differ based on pressure settings of ventilator, type of aerosol devices and their position in the circuit.

METHODS AND MATERIALS

The experimental design is shown in Figure 1.

The BiPAP ventilator was set as S/T mode, non-humidified, RR 20 breaths/min, I:E ratio 1:2, and inspiratory/expiratory positive airway pressure (IPAP/EPAP) of 10/5, 15/5 or 15/10 cm H_2O, respectively. Tidal volume (V_T) was maintained at ~300 ml by adjusting the test lung.

Six ml albuterol sulfate solution (2.5mg/ml), or 8-30 puffs albuterol sulfate aerosol (90μg /puff) at an interval of 15 seconds, were administered via a vibrating aperture plate (VAP) and a jet nebulizer, or a pressurized metered-dose inhaler (pMDI) with spacer chamber, respectively.

Three experiments were performed for each of the 3 aerosol devices, at each of the 3 positions and under each of the IPAP/EPAP settings. Drug was captured on a filter, eluted and quantified by spectrophotometry (276 nm).

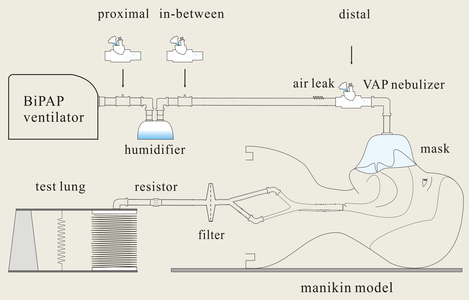

Figure 1. Experimental schematic of aerosol delivery during NIV.

RESULTS

The efficiency of aerosol delivery varied from 0.43±0.12% to 10.01±1.32% of the nominal dose, depending on the type of aerosol device and its position in the circuit. (Figure 2).

Aerosol generators placed at the distal position showed the highest efficiency of aerosol delivery compared to those at in-between or proximal position (P<0.001), and the VAP nebulizer was more efficient than the jet nebulizer and pMDI (6.1±2.9% vs. 3.68±1.06% and 1.05±0.73%, F=111.92, P<0.001).

The IPAP/EPAP settings had lesser influence on the efficiency of aerosol delivery as shown in Table 1.

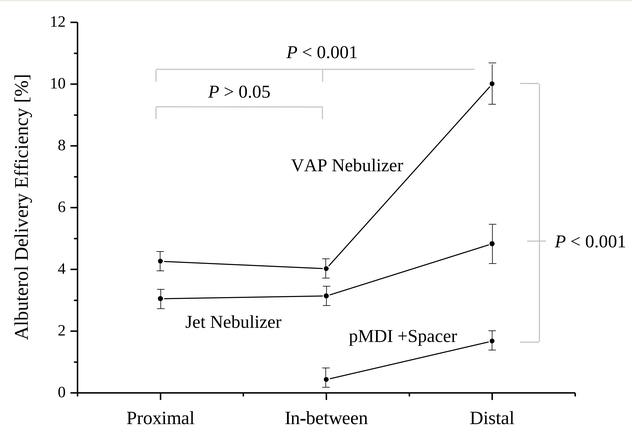

Figure 2. Effects of aerosol devices and their positions in the circuit on the efficiency of albuterol aerosol delivery, expressed as % of nominal dose.

DISCUSSION

High inspiratory flow rate and increased turbulent flow during noninvasive ventilation caused greater impaction and sedimentation of aerosol particles into the tubing, resulting in significant variability of the efficiency of aerosol delivery to the lower respiratory tract, based on the placement of aerosol devices in-line in the circuit.

The "charging effect" of the facemask and less expiratory waste of aerosol increased drug delivery when the aerosol generators were placed at distal position (between the mask and exhalation port).

Compared to pMDI, the unique characteristics of VAP nebulizer to produce low velocity aerosol particles and minimal drug residual volume enhanced aerosol delivery.

Rapid shallow breathing pattern and lower tidal volumes appeared to negate the effect of higher positive pressure support settings on aerosol delivery.

CONCLUSIONS

During noninvasive ventilation, aerosol delivery with different aerosol generators showed significant variability.

A VAP nebulizer placed distal to the air leak in the circuit had a higher efficiency than a jet nebulizer or pMDI.

The efficiency of aerosol delivery with a pMDI would need to be significantly enhanced for this delivery method to be practical for clinical use during noninvasive ventilation.

Table 1. Effects of ventilator settings on the efficiency of aerosol delivery.

Devices	IPAP/EPAP 10/5 (cm H_2O)		IPAP/EPAP 15/5 (cm H_2O)		IPAP/EPAP 15/10 (cm H_2O)		P Value
	Albuterol (μg)	Efficiency (%)	Albuterol (μg)	Efficiency (%)	Albuterol (μg)	Efficiency (%)	
VAP	384.07±189.38	6.40±3.16	336.52±115.15	5.61±1.92	381.07±205.05	6.28±3.45	0.56*
Jet	201.52±53.63	3.35±0.89	211.83±40.21	3.53±0.67	249.74±83.3	4.14±1.36	0.02#
pMDI	15.79±4.96	1.35±0.94	19.36±8.84	1.01±0.61	16.59±5.70	0.80±0.48	0.07*

•Analysis of variance shows insignificant differences in the efficiencies under 3 levels of IPAP/EPAP settings (P > 0.05). # Least significance difference tests shows significant differences between IPAP/EPAP 15/10 Vs. 15/5, and IPAP/EPAP 15/10 vs. 10/5 cm H_2O settings (P < 0.05). IPAP/EPAP: inspiratory/expiratory positive airway pressure. %: percent of nominal dose.

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