IMPROVING AEROSOL DELIVERY TO INFANTS DURING NASAL CPAP: AN IN VITRO MODEL

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INTRODUCTION

Historically, aerosol delivery to pre- and near-term infants by nebulizers has been inefficient with less than 1% deposition of the nominal dose, on or off the ventilator (Fink, Resp Care 2004).

Aerosol delivery to infants using nasal continuous positive airway pressure (nCPAP) has not been reported using high efficiency aerosol delivery systems. We created an in vitro model of infant ventilation during nasal CPAP to compare the efficiency of two aerosol delivery devices, the Aeroneb® Professional Nebulizer System (Aeroneb Pro) and a low volume prototype Pulmonary Drug Delivery System (PDDS) suitable for placement proximal to the infant's airway (FIGURE 1). Both devices incorporate Aerogen's OnQ™ micropump aerosol generator (FIGURE 2).

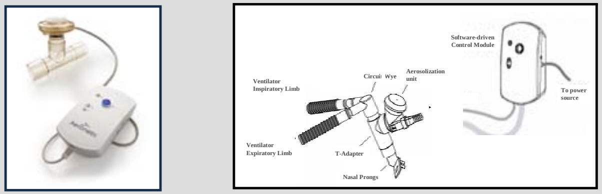

FIGURE 1: THE AERONEB® PROFESSIONAL NEBULIZER SYSTEM (LEFT). THE PULMONARY DRUG DELIVERY SYSTEM (PDDS) FOR NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE (nCPAP: RIGHT).

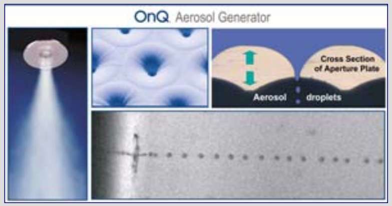

FIGURE 2: THE AEROGEN ONQ™ AEROSOL GENERATOR WITH THE GENERATOR (LEFT PANEL), A MICROSCOPIC VIEW OF TAPERED APERTURES (UPPER MIDDLE), AND CROSS SECTION OF APERTURES (UPPER RIGHT). HIGH SPEED MICROSCOPIC PHOTOGRAPH OF AEROSOL GENERATED FROM A SINGLE APERTURE (LOWER RIGHT).

OBJECTIVE

We wanted to determine the effect of aerosol generator placement in the inspiratory limb and proximal to the patient airway on delivery of drug to the distal tip of the nasal prongs of an nCPAP during simulated infant ventilation. A secondary objective was to differentiate delivery of aerosol vs condensate to the infant model.

MATERIALS AND METHODS

A lung simulator, consisting of an adapter with orifices representing infant size nares connected to an absolute filter, and attached to a reciprocating pump animal ventilator (Harvard Apparatus), was set to infant ventilatory parameters (VT 10 mL, resp rate 40 bpm). Drug was collected on a filter placed distal to the nasal prongs, and assayed using HPLC.

A constant air flow of 10 L/min was used to generate a CPAP of 5 cm H_2O. Albuterol sulfate (0.5 mL; 0.5%) was aerosolized with an Aeroneb Pro placed in the inspiratory limb of the nCPAP circuit, and with a PDDS nebulizer placed between the main flow of the nCPAP circuit and the nasal prongs, above the level of the filter (n=3).

To differentiate between aerosol and condensate delivery to the filter, an additional set of runs was performed with the PDDS below the filter (n=5).

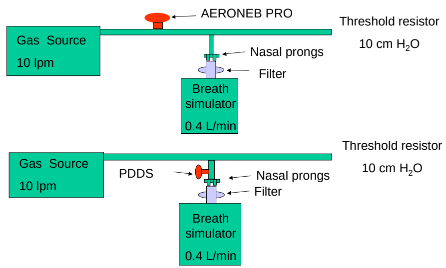

FIGURE 3: DIAGRAM OF MODEL USED FOR MEASURING AEROSOL DELIVERY WITH SIMULATED INFANT BREATHING PATTERN DURING NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE (nCPAP). TOP: THE AERONEB PRO (TOP) PLACED IN INSPIRATORY LIMB OF nCPAP WITH AEROSOL DILUTED BY TOTAL FLOW OF GAS PASSING THROUGH NEBULIZER. BOTTOM: THE PULMONARY DRUG DELIVERY SYSTEM (PDDS) PLACED BETWEEN THE PRIMARY GAS FLOW AND SIMULATED PATIENT AIRWAY.

FIGURE 4: MODEL USED FOR MEASURING AEROSOL DELIVERY WITH SIMULATED INFANT BREATHING PATTERN DURING NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE (nCPAP). THE PULMONARY DRUG DELIVERY SYSTEM (PDDS) PLACED ABOVE THE FILTER (LEFT) AND BELOW THE FILTER (RIGHT).

RESULTS

Placement of the Aeroneb Pro in the inspiratory limb of the nCPAP circuit, resulted in deposition (mean ± SD) of 1.3±0.8% of the albuterol dose placed in the nebulizer.

By contrast, placement of the PDDS between the gas flow through the CPAP circuit and the simulated patient airway, above the level of the filter yielded 22.5 ± 1.7% deposition. When the PDDS was placed below the filter, deposition was reduced to 12.8±2.7%.

SUMMARY

The PDDS at the airway delivered an order of magnitude more albuterol through the nasal prongs to the filter during nCPAP than the Aeroneb Pro when placed in the inspiratory limb of the circuit (typical placement).

We used the Aeroneb Pro because it is a highly efficient nebulizer that has been shown to be more efficient than standard jet nebulizers in an animal model of infant ventilation (Dubus, AJRCCM 2003). In this nCPAP model, the low deposition with even a high efficiency nebulizer is due in large part to the dilution of the aerosol output of the Aeroneb Pro by the total flow of gas (10 L/min) passing through the nebulizer.

The ability to place the PDDS between the primary gas flow and the patient airway reduces dilution of aerosol from 10 L/min (total flow through the circuit) to approximately 0.4 L/min (minute ventilation of the infant simulator). This reduction in aerosol dilution appears to be inversely related to increasing deposition.

Our data from placement of the PDDS above the filter suggests that up to 40% of the albuterol delivered to the model in a standard orientation (nebulizer above the patient) may be condensate dripping from the nasal prongs and circuit into the filter instead of aerosol. In estimating aerosol dose delivery *in vitro* it is important to differentiate aerosol dose inhaled from drug condensate that is instilled.

CONCLUSION

Placement of the aerosol generator proximal to the patient airway is a key component for improving aerosol efficiency in this model of nCPAP. The high efficiency delivery of aerosol to this nCPAP infant model suggests future opportunities for administration of active medications to the airways of infants.

Additional work is anticipated to establish *in vitro* / *in vivo* correlation with this model of nCPAP with infant ventilation.

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