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Bronchodilator Delivery During Simulated Pediatric Noninvasive Ventilation

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Abstract

Introduction: Noninvasive Ventilation (NIV) is usually applied using Bi-Level Positive Airway Pressure (Bi-PAP) devices and many of these devices use a single-limb patient circuit with an integrated leak port to purge the circuit of exhaled carbon dioxide. Sometimes, bronchodilator therapy is indicated in pediatric patients. However, there have been no forthcoming studies in the literature describing the optimal nebulizer position, with respect to leak during pediatric NIV. We hypothesized that there were no differences in albuterol delivery with a vibrating mesh nebulizer between three different positions/exhalation leak valve combinations within the patient circuit during simulated pediatric NIV. **Methods:** A simulated upper airway model was attached to a spontaneously breathing lung model (ASL 5000, Ingmar medical). A noninvasive ventilator equipped with heated wire circuit and heated humidifier was attached to the simulated patient via a pediatric oronasal mask. Albuterol (5 mg) was delivered with vibrating mesh nebulizers and at three different circuit position/leak condition combinations, including: 1) prior to the humidifier and leak valve; 2) between the humidifier and leak valve; and 3) integrated within the mask and after the leak. Albuterol was recovered from a filter and quantified using high-pressure liquid chromatography. **Results**: Greater Albuterol mass was delivered to the filter with the NIVO® nebulizer integrated into the mask than any other testing condition ($P<0.01$). In the conditions where the nebulizer was placed prior to the exhalation leak valve, greater drug delivery was observed when the nebulizer was placed proximal to the mask (Position 2) than when placed prior to the humidifier (Position 3, $P<0.01$). **Conclusion**: Albuterol delivery during simulated pediatric NIV is affected by the position of the nebulizer in relation to the expiratory leak valve and the distance the nebulizer is placed from the filter. A vibrating mesh nebulizer placed intra mask may provide a better alternative for medication delivery than those previously used during pediatric NIV.

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Introduction

Noninvasive ventilation (NIV) is increasingly used as an alternative to invasive ventilation in pediatric patients, including those with asthma. NIV provides relief from airway obstruction in children by physically stenting airways open during the respiratory cycle, reduces work of breathing and auto-PEEP, and increases alveolar ventilation. Obvious benefits include ability for patient to communicate, lack of a high resistance artificial airway, decreased bronchial irritation and need for sedation, and elimination of ventilator acquired pneumonia risk.[1] NIV is associated with improved mortality for adult patients with COPD and other forms of respiratory distress. [2-12] One randomized controlled trial [13] and several small observational studies[14-16] demonstrate NIV is a safe and effective option for supporting children with respiratory failure, including patients with asthma not responding to conventional therapies.

Bi-Level Positive Airway Pressure (Bi-PAP) is a common NIV mode being used in pediatrics in the PICU. Many BiPAP devices use a single-limb patient circuit with an integrated fixed-leak port "expiratory valve" and high flows to purge the circuit of exhaled carbon dioxide. A major concern with administering aerosolized drugs in this system is whether the combination of high system flows and leak actually results in any aerosolized drug delivery to the patient. Additionally, there are several other factors influencing the efficiency of aerosol delivery during NIV. These include: (1) type of ventilator, (2) mode of ventilation, (3) circuit humidity, (4) type of interface, (5) type of aerosol generator and its configuration, (6) drug related factors, including aerosol particle size, (7) breathing parameters, and (8) patient-related factors; including the level of respiratory distress, hemodynamic status, the type and severity of lung disease, and synchronization of aerosol generation with inspiratory airflow[17]. Also, the ability to tolerate a facemask, the quality of mask fit, the degree of leak around the mask and position of the exhalation leak valve in NIV circuitry all may impact drug delivery.

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Until recently, nebulizer and leak valve position in the circuit could not be moved for technical reasons. New developments include facemasks with interchangeable leak adapters, vibrating mesh (VM) nebulizers, which add no flow to the circuit, and the very recent introduction of a lightweight VM nebulizer that can be integrated proximal to a pediatric oronasal mask, all which allow variations to the standard NIV circuit set up. We sought to test the null hypothesis that there are no differences in albuterol delivery between a standard VM nebulizer placed 1) before the humidifier and before the leak, 2) after the humidifier and before the leak and 3) an integrated mask VM nebulizer placed after the leak.

Methods

This study was designed, performed, and data were analyzed at the Seattle Children's Hospital Respiratory Therapy Department, Seattle WA under the direct supervision of the senior author (RMD). The first author (CW) was present for the study design, acquiring data, analyzing data, and for the entire process of writing the manuscript. NIVO® aerosol devices were donated by Trianim and laboratory supplies were purchased with funds from a research grant provided by the Center for Developmental Therapeutics, Seattle Children's Research Institute; Seattle, WA.

Pediatric Upper Airway and Lung Model

A pediatric upper airway and lung model was devised by attaching a pediatric resuscitation head with a simulated face and oronasal cavity (Little Junior; Laerdal Medical) to a 5.5 mm ID endotracheal tube connected to a simulated spontaneously breathing lung model designed to simulate a child with asthma (ASL 5000, Ingmar medical). The test lung was configured with mechanics that have been previously observed in children with severe status asthmaticus.[18,19] Settings were: compliance 20 mL/cmH_2O, resistance 15 cmH_2O/L/s, respiratory rate 30/min and inspiratory muscle pressure was adjusted to obtain tidal volume 180 mL during NIV. The test lung was also configured to mimic active exhalation by setting the expiratory muscle pressure to 5 cmH_2O. Two bacterial/viral electret filters

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(Respirgard-II, Vital Signs; Englewood, Colorado) were connected in series between the 5.5 mm ID endotracheal tube and the lung model. One filter was used to capture the inspired drug and a second filter was used to protect the internal components of the lung model (Figure 1).

Ventilator and Humidification

A V60 Bi-PAP ventilator (Phillips Respironics, Carlsbad, CA), equipped with heated wire circuit, Fisher and Paykel 850 heater (Auckland, NZ), expiratory leak-valve and facemask was attached to the pediatric resuscitation head. The ventilator settings were BiPAP S/T mode: IPAP 16 cmH_20, EPAP 8 cmH_20, FIO_2 0.50, Rise Time-2, and Autotrak trigger. A size small AF531 (Phillips Respironics, Carlsbad, CA) oronasal facemask with interchangeable "fixed orifice" leak port elbow adapters was firmly secured to the face of the model. Tidal volume (~180 mL) was confirmed prior to and during all testing to assure an adequate mask seal. The circuit and system was heated to approximately 35°C and the lung model was warmed to 37°C for twenty minutes prior to testing. These temperatures were maintained throughout the entire study.

Nebulizers

New Aeroneb Solo VM (Aerogen, Mountain, CA) and NIVO® (Phillips Respironics, Carlsbad, CA) nebulizers were used for testing. Both are vibrating mesh (VM) nebulizers that can be placed in-line during NIV. The NIVO® is a novel light-weight VM nebulizer designed specifically for NIV that attaches to an adapter in the face mask (Figure 2). A Pro-X controller (Aerogen, Mountain, CA) was used to power all the nebulizers.

VM nebulizers are highly efficient[20] providing nearly 2-4 times greater drug delivery than jet nebulizers during pediatric mechanical ventilation.[21] They also allow medication to be delivered without having to disconnect the patient from positive pressure, can remain in-line when not being used, and in some cases, can be configured to provide continuous bronchodilator therapy. Unlike jet nebulizers, no flow is added to the patient circuit by the VM nebulizers. Avoiding the addition of extra flow into the circuit may prevent patient-ventilator dys-synchrony from ineffective triggering that often occurs in small pediatric patients or hyperinflated asthmatic patients with auto-PEEP.

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Nebulizer Positions

In position 1 (pre-humidifier, pre-leak), the Aeroneb Solo was placed on the dry side of the heated humidifier and a #2 standard leak adapter elbow (Phillips Respironics, Carlsbad, CA) was attached to the facemask. In position 2 (post-humidifier, pre-leak), the Aeroneb Solo was placed after the heated humidifier and just prior to the #2 standard leak adapter elbow and facemask. In position 3 (post-leak, intra-mask), the NIVO® nebulizer was attached to the mask using a #1 standard leak NIVO® entrainment elbow (0% Leak) and the #2 standard leak entrainment elbow was removed and replaced with a standard disposable exhalation valve (DEP; Phillips Respironics, Carlsbad CA) in the circuit.

Continuous expiratory leak was observed on the V60 with the proximal pressure line (no data). Calculated leak during the testing was similar between the standard disposable exhalation valve and the standard #2 leak entrainment elbow.

Medication Delivery

The nebulizers were placed into each of the three respective positions and the system heat and humidification was allowed to stabilize prior to testing at each condition. Albuterol (5 mg) was drawn up with a 1mL pipette and mixed with 2.5mL of normal saline for a total solution volume of 3.5 mL, placed into the nebulizer, and nebulized into the circuit. Three doses of albuterol were given in each of three nebulizers tested at each of the circuit positions (n=9 measurements at each location or n=27 total). Testing was completed when all of the solution was nebulized. The bacterial/viral electret filter at the end of the endotracheal tube was removed, labeled and recorded in a laboratory notebook and placed into a refrigerator. The face of the upper airway model was dried between each change in nebulizer position and fluid accumulation in the upper airway was eliminated to reduce the likelihood of large drug molecules reaching the filter. The mask was secured to eliminate any system leaks, based upon tidal volume delivery (180 mL) to the lung model and calculated leak. All data regarding lung model triggering as well as volume, pressure, flow and graphical waveform analysis were sampled at 500 HZ and stored within the ASL 5000 software package (version 3.2). These data were later analyzed

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to determine whether nebulizer performance and excessive fluid condensation affected triggering under all of the testing conditions.

Albuterol Measurement

Albuterol was recovered from the bacterial/viral electret filter following nebulization at each position and quantified using high-pressure liquid chromatography. The filters were eluted by 20 mL methanol, shaken and thoroughly withdrawn under negative pressure. The elution liquid was collected in 50 mL centrifuge tubes. The samples were dried with nitrogen gas flow. The residue was reconstituted by adding 200 μL of acetonitrile/water (1:1) to each sample. The samples were analyzed by HPLC with UV detection. The Agilent 1100 HPLC system was equipped with a quaternary pump, diode array detector, and Agilent (Santa Clara, CA) precolumn (C18, 2 μm) and analytical columns (XDB-C8, 46 × 150 mm, 5μm). The mobile phase was methanol-20 mM potassium phosphate buffer pH 3.0 (5:95) and the flow rate was 1 mL/min. The detector wavelength was set at 278 nm. Twenty microliters of each sample was injected into the HPLC system. The retention time was 16.5 min. The residual albuterol in the filters was quantified by a standard curve range from 0.25 mg/mL to 3.0 mg/mL Albuterol recovery was measured with a known concentration prior to the experiment and approximately 100% of the nominal dose of albuterol was recovered from the filter using the aforementioned recovery method.

Statistical Analysis

Albuterol concentrations were recorded in an Excel (Microsoft, Redmond, WA) spread sheet. All data were expressed as mean±SD and percent of nominal dose placed into the nebulizer. Statistical Analyses were performed in SPSS (version 20). A one way Analysis of Variance (ANOVA) was used with a Tukey test for *post-hoc* analysis to compare differences between the mean delivered albuterol mass at the three circuit position/leak conditions. Statistical significance was set a *priori* at $p < 0.05$.

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Results

Albuterol delivered to each filter was expressed in absolute terms (Figure 3) and as a percentage of the nominal dose (5mg Albuterol; Figure 4) at each position. There was greater albuterol delivered to the lung model filter with the NIVO® VM nebulizer placed at the mask (Position 3) than the other two other testing conditions ($P<0.01$). In the conditions using the Aeroneb Solo nebulizer, greater drug delivery was observed when the nebulizer was placed between the leak valve and the humidifier (Position 2) than when the nebulizer was place between the ventilator and humidifier (Position 1), $p<0.01$.

With the nebulizer in Position 3, a large amount of albuterol was being emitted from the disposable exhalation port during inspiration that wasn't observed during the other two testing conditions (Figure 4). All BiPAP NIV breaths were triggered by the lung model. There were no differences between delivered inspiratory pressures, tidal volume, or PEEP related to the operation of the VM nebulizers.

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Discussion

Over the last decade, technologic improvements in nasal and oronasal mask interfaces have allowed successful application of NIV in pediatric patients with severe respiratory distress of different etiologies. Despite limited experimental data, clinicians implement NIV in children with asthma in the Pediatric Intensive Care Unit (PICU) both as an early intervention and as a "rescue" strategy to prevent endotracheal intubation and invasive ventilation. This practice is guided by very little evidence other than approaches previously describe in the adult literature.

Patients with asthma require large amounts of inhaled bronchodilators and systemic steroids administered within a relatively short period of time. Thus, timely and effective delivery of bronchodilator therapy can play a significant clinical role in reducing airway obstruction, ventilatory impairment, and respiratory distress[7-9]. Studies *in vitro* suggest greater aerosol drug delivery during NIV than when no positive pressure is applied to a lung model.[8] Studies in children with Cystic Fibrosis have demonstrated 30% greater bronchodilator delivery following nebulization provided with NIV than following nebulization without NIV[22]. Thus, NIV may improve bronchodilator delivery and transiently reduce respiratory distress until other pharmacotherapy has been given time to have a clinical effect.

The major finding of the current study was that albuterol delivery during simulated pediatric NIV is dependent upon both location of the nebulizer and location of the fixed expiratory leak in the single-limb BiPAP circuit. We observed between a 200-300% greater drug delivery with the NIVO® VM nebulizer than the other two commonly used VM nebulizer configurations. We believe these results are related less to the type of VM nebulizer and more to the fact that the nebulizer was placed after the leak valve which ultimately allowed more drug delivery to the filter and less to the circuit and/or atmosphere.

There have been three *in vitro* studies [23-26] and two clinical studies[22,27], that have evaluated drug delivery during adult NIV. There has been only one pediatric NIV study and this combined *in vitro/in*

vivo study[22] was designed to evaluate differences in aerosol delivery with and without NIV. Nonetheless, there are very few objective data to guide clinicians when selecting an optimal device or approach for aerosol drug delivery during pediatric NIV. It would be very difficult to extrapolate from the findings of adult NIV aerosol studies and assume similar results in a pediatric patient. Pediatric patients have smaller tidal volumes, higher respiratory rates, lower I:E ratios and smaller airway passages than adults. Previous studies have suggested that all of these factors in infants and small children contribute to lower inhaled drug delivery than adults[28,29]. In both intubated and non-intubated pediatric patients, aerosol deposition is suggested to be <1% of the nominal drug dose compared to 8-22% in adults[28].

We suspect that a major reason why no additional pediatric-specific NIV aerosol studies have been recently described in the literature is due in part to technological limitations of available pediatric nebulizers and NIV mask interfaces. Until very recently, many of the mask interfaces used in this population were prepackaged with the leak exhalation port integrated into the NIV mask, making it physically impossible to place a nebulizer between the leak and the mask during pediatric NIV. Moreover, the weight and awkwardness of placing available aerosol delivery devices inline may place unnecessary tension on the mask resulting in greater leaks and lower drug delivery to the patient. The lightweight NIVO® VM nebulizer represents a suitable new technology that obviates many of the previous concerns related to pediatric drug delivery during NIV.

Adult studies with similar designs have focused on aerosol delivery using novel NIV mask technologies. Branconnier et al[24] compared drug delivery during simulated adult NIV using two different mask types; one with an integrated mask leak port and a newer mask version that used a leak elbow that could be adapted to the patient circuit. The latter configuration made it possible for investigators to adapt a jet nebulizer after the leak. Similar to our findings, Branconnier reported greater drug delivery when the jet nebulizer was placed between the leak and the mask. It is interesting to note that the Albuterol mass was similar between the jet nebulizer used by Branconnier et al.[24] and the VM

nebulizer used in the current study when compared at the respective pre/post leak conditions. Despite the smaller tidal volumes, lower transit times for aerosol delivery, and the use of a heated humidifier in our pediatric lung model, we believe that the reason why we observed similar findings to the previously described adult lung model study[24] is because the VM nebulizer may be more efficient than a jet nebulizer.[22] Thus, we are not surprised to learn that albuterol delivery, expressed per unit of body weight, is much greater during pediatric NIV comparing data from these two studies. We also chose to use a heated humidifier during this study; whereas most adult NIV studies have not. The application of heated humidity to the patient circuit is an important factor affecting aerosol delivery. Unlike the Branconnier study, we did not test drug delivery without a heated humidifier but based on a previous study[30], aerosolized albuterol delivery is likely to be a approximately 200% greater when humidity is not being applied.

Adding humidification to the NIV circuit may be preferred with asthmatics due to underlying airway inflammation and high potential for mucous plugging[17]. Administering high gas flow rates without humidity may overwhelm the capabilities of the nose and upper airway to properly humidify gas resulting in drying of airway passages which may lead to consequent increased nasal resistance, and potential for increased airway reactivity[17]. As such, high bronchodilator dosages may need to be increased when humidification is added due to the potential to decrease aerosol delivery by as much as 40-50% [18]. These findings also raise the questions about whether heated humidifiers should be turned off intermittently or bypassed while aerosolized drugs are being administered during NIV. While this practice cannot be routinely recommended at this time, it should encourage additional research.

Many clinicians from pediatric institutions commonly place nebulizers between the ventilator and the humidifier during all forms of ventilation, including NIV. There is anecdotal evidence that this not only reduces the level of condensation in the circuit but also results in better drug delivery. In two recent reports, Ari and colleagues evaluated bronchodilator delivery during simulated pediatric[21] and adult ventilation[30] using a VM nebulizer at two different locations. In this study,[30] there was nearly a

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200% increase in drug delivery when the VM nebulizer was placed between the ventilator and the humidifier during simulated adult ventilation. However, based on the pediatric study[21] it is unclear whether there were any significant differences in aerosol delivery between these two positions.

We observed a significant reduction in medication delivery when the VM nebulizer was moved from Position 2 or Position 3 to Position 1 (between the ventilator and humidifier during NIV). There are major and notable differences in the circuit configuration used during NIV and conventional ventilation. The circuits used by Ari et al.[21] are dual-limb pediatric circuits and those used in the present study used a BiPAP specific single-circuit configuration. The gas flow dynamics of a single-circuit may be more complex than a dual-limb circuit because high gas flows coupled with a common inhalation/exhalation pathway are likely to cause higher turbulence in the system. Thus, we believe that the poor drug delivery observed when the VM nebulizer was placed back at the BiPAP ventilator may be multi-factorial. It is likely that the use of high flows may dilute the aerosol bolus being emitted from the nebulizer into the circuit. Also, these high flows may increase the inertial activities of aerosol particles resulting in drug impaction in the humidifier and along the length of the patient circuit. As such, the beneficial "reservoir-like" effects of the dual-limb circuit, observed by Ari et al.[21] do not readily apply to a single-circuit NIV configuration. This issue is further complicated by the fact that many ventilator companies are now integrating pediatric-specific NIV algorithms into standard ICU ventilators that use a dual-limb circuit. Thus, additional studies are needed to compare medication delivery with all availa ble devices that are being used in the PICU to provide NIV.

Chatmongkolchart et al.[26] evaluated medication delivery in an adult lung model using a jet nebulizer and a single circuit BiPAP ventilator. Similar to our findings and at comparable peak pressures, they observed a two-fold greater increase in drug delivery when the nebulizer was moved away from the BiPAP ventilator and placed after the leak port and proximal to the face mask. Calvert et al[25] nebulized Salbutamol with a jet nebulizer at three similar positions during simulated adult NIV.

Like our study and previous studies, drug delivery was half the value when the nebulizer was placed back at the ventilator compared with proximal to the patient.

Abdelrahim et al. conducted both an *in vitro* study[23] and a randomized cross-over clinical study[27] comparing aerosol delivery with a VM nebulizer, (Aerogen Pro) to a jet nebulizer at two positions within the patient circuit (Pre and Post Leak). Regardless of the nebulizer being used, they also observed nearly 200% greater drug delivery when the nebulizer was placed post-leak. In this study, drug mass was also analyzed coming out the leak port at both pre and post leak conditions. A greater amount of drug was emitted from the leak port in the pre-leak condition than the post-leak condition. However, nearly 20% of the nominal dose of albuterol was recovered from the leak port when the nebulizer was placed after the leak. They state, "For position A (between the leak valve and lung simulator), therefore, all the dose that is aerosolized during the inhalation phase is directed to the inhalation filter." While we did not measure aerosol emitted from the leak port during this study, a plume of aerosol (Figure 5a) could be visualized during inhalation, even when the nebulizer was placed after the leak. Also, based on Figure 5b the point at which the leak is the greatest using the V60 BiPAP ventilator is at the peak inspiratory pressure. Thus, it is likely that a large fraction of drug is being lost during inhalation. This raises many questions about whether the position of the leak valve in the circuit may influence drug delivery differently during NIV. Future studies would need to be conducted to answer this question and determine if placing the leak valve distal to the patient has any effect on carbon dioxide elimination during NIV. We also cannot rule out other confounding variables that may have contributed to differences in drug delivery between the different positions, including different tubing distances or the fact that two different types of VM nebulizers were used.

Even though the majority of these *in-vitro* studies pertain to adults, each of the studies used a similar circuit configuration, BiPAP ventilator, and in one case[23] a similar nebulizer to the one used in the current study. Our findings suggest there are differences in drug delivery related to the position of the leak with respect to the leak-port and circuit position that mirror previous observations in aerosol

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studies using an adult lung model and NIV. Based on these data, clinicians that are not able to place the nebulizer after the leak, may benefit more from having it placed just prior to the leak than back at the ventilator.

Limitations

In this in *vitro study*, we took careful measures to simulate a realistic pediatric clinical environment. This approach was different from those reported in previous NIV aerosol studies. We used modern BiPAP ventilators and nebulizers, a heated humidifier, a realistic face model with oronasal passages, and a heated, actively breathing test lung configured with mechanics values similar to those measured in pediatric asthmatics. However, like all data obtained from aerosol studies in vitro, the results must be approached with some trepidation. The amount of drug delivered to the filter represents the total mass of available drug delivered to the airways, but it doesn't take into account the amount of respirable drug particles that may be delivered to the peripheral airways of the lungs and where they are needed most. Thus, it is extremely important to mention that, despite making every attempt to avoid large droplets of accumulated liquid medication (combined with humidity) from reaching the filter, it is still possible that this fluid can condense anywhere in the airway model and be delivered to the filter media during inhalation. We also noted that as the nebulizer was placed closer to the simulated patient, there appeared to be more condensation in the mask and circuit. This fluid tended to pool and could not be observed entering the oral or nasal airway openings. Thus is it unlikely, based on the variability of albuterol mass (SD), that large droplets were introduced into the filter.

Additional limitations include using only one particular brand of BiPAP ventilator, humidifier, circuit, and mask. We also used one lung model configuration and a single combination of NIV settings on the BiPAP ventilator. Finally, we only tested one particular type of nebulizer. We did not compare the VM nebulizer to jet nebulizer or a pressurized meter-dose inhaler/spacer. There are currently no approaches that allow placing these devices after the leak-port while still maintaining the nebulizer in a

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vertical position while minimizing unnecessary torque on the face-mask. Improvements in device technologies and additional research are needed to determine whether changing these variables has any effect on patient comfort or aerosol delivery during simulated pediatric NIV.

Conclusion

Based on these findings, it would seem that clinicians should avoid placing the nebulizer back at the ventilator. The NIVO® nebulizer represents an efficient lightweight nebulizer that can be easily integrated into a pediatric NIV mask without creating unnecessary torque and compromising the seal. If these bench data can translate into clinical practice, then the NIVO® VM nebulizer may represent a novel approach for providing more timely and efficient drug delivery to pediatric patients receiving NIV for respiratory failure.

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Figure Legend

Figure 1.

Experimental set-up

A pediatric upper airway and lung model was devised by attaching a pediatric resuscitation head with a simulated face and oronasal cavity (Little Junior; Laerdal Medical) to a 5.5 mm ID endotracheal tube connected to a simulated spontaneously breathing pediatric asthmatic lung model (ASL 5000, Ingmar medical). Two bacterial/viral electret filters (Respirgard-II, Vital Signs; Englewood, Colorado) were connected in series between the 5.5 mm ID endotracheal tube and the lung model. A V60 Bi-PAP ventilator (Phillips Respironics, Carlsbad, CA), equipped with heated wire circuit, Fisher and Paykel 850 heater (Auckland, NZ), expiratory leak-valve and facemask was attached to the pediatric resuscitation head. Following a brief temperature stabilization period, 5 mg of Albuterol was nebulized three times at each of the three positions using three new nebulizers (n=27 measurements) and filters were collected.

Figure 2A and B

Phillips AF531 mask with interchangeable elbow and aerogen NIVO® nebulizer assembled (A) and disassembled (B)

Figure 3.

Delivered Albuterol Mass

All experiments were conducted using 5 mg Albuterol. Values represented as mean±SD Albuterol delivered to filters for 3 runs per nebulizer at 3 locations. Data not sharing similar symbols are different, $p<0.05$.

Figure 4.

Delivered Albuterol expressed as a percentage of nominal dose

All experiments were conducted using 5 mg Albuterol. Values represented as percentage of the nominal dose (5 mg Albuterol) for 3 runs per nebulizer at 3 locations.

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Figure 5.

Effects of inspiratory pressure on leak and aerosol delivery

A plume of nebulized Albuterol can be observed leaving the leak port, with the NIVO® nebulizer in position 3, during inhalation which suggests that even though the nebulizer is placed after the leak, a significant amount of drug is still exiting through the leak valve adaptor. Figure 4B shows a pressure/time scalar (upper) and a leak/time scalar (lower) recorded by the V60 from an actual patient receiving BiPAP. It can be noted that the leak is proportional to pressure and thus, is greatest during the peak inspiratory pressure. As such, it is possible that a greater proportion of aerosol is leaving the system during inhalation than during exhalation.

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Figure 1

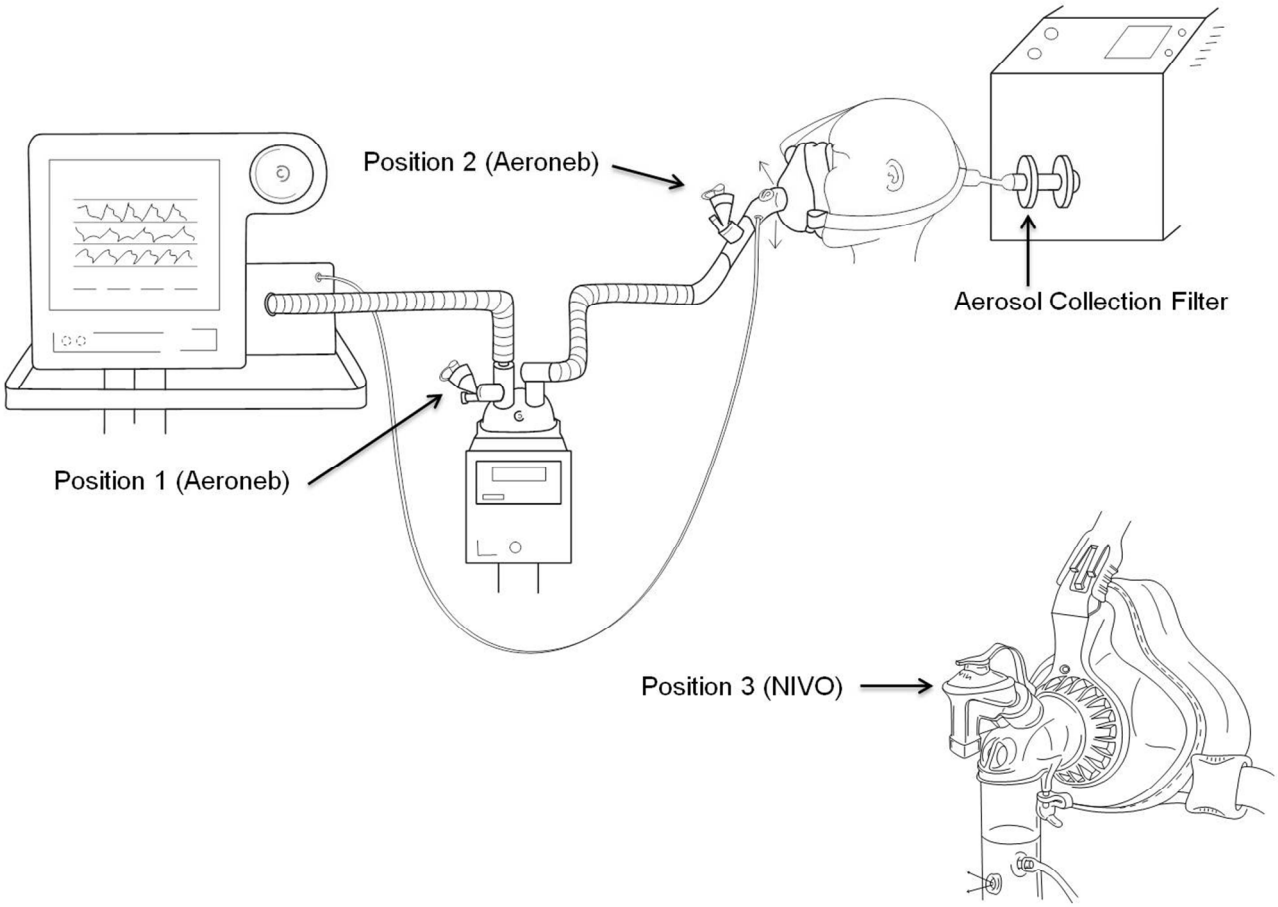

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Figure 2A

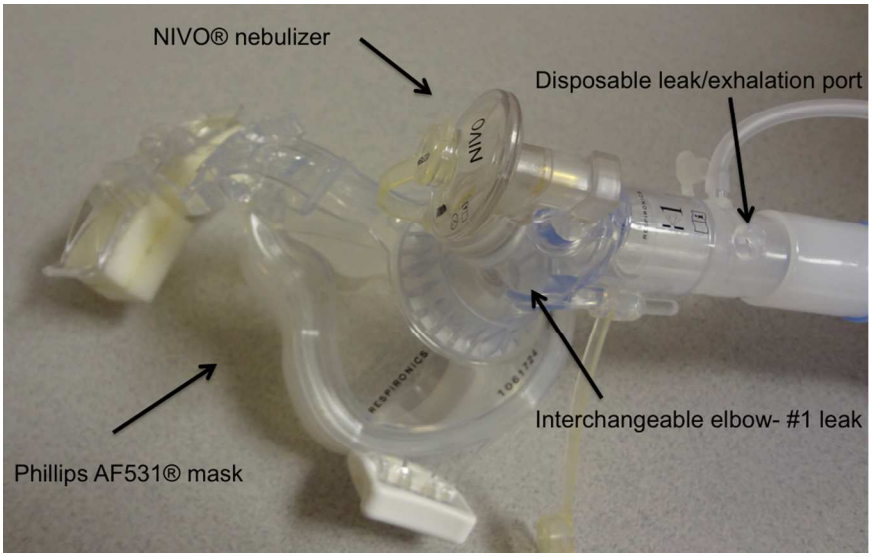

Figure 2B

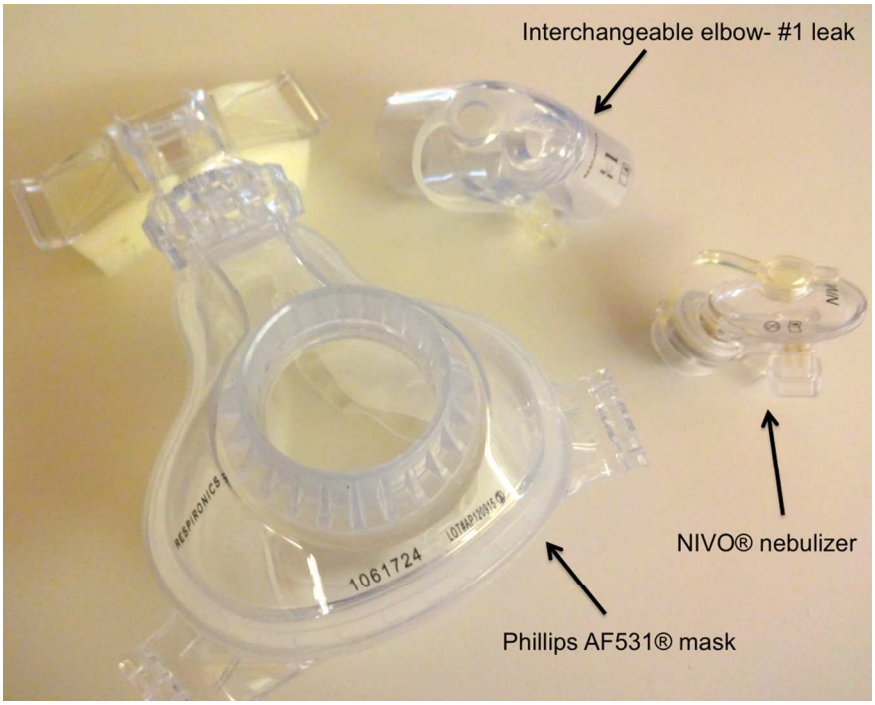

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Figure 3

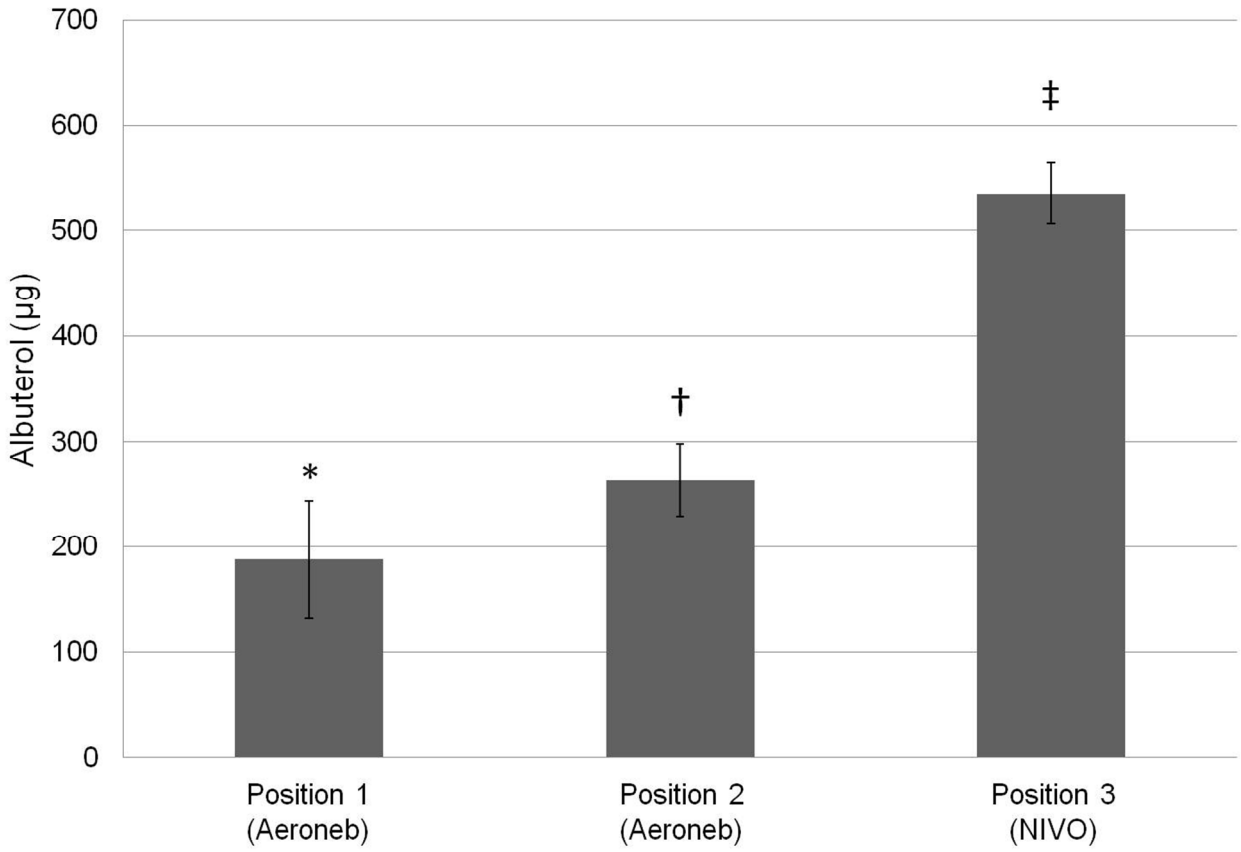

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Figure 4

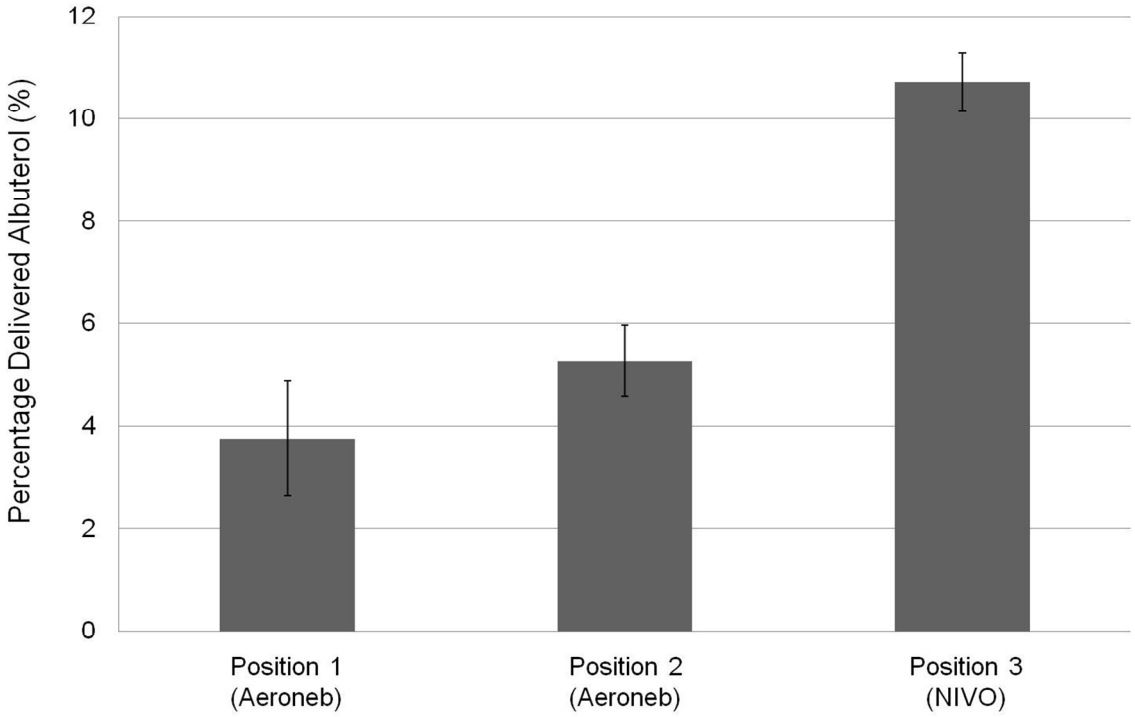

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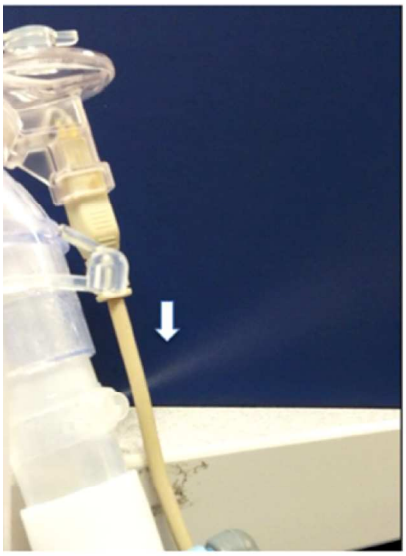
Figure 5

5A



5B