

Georgia State University
ScholarWorks @ Georgia State University

Respiratory Therapy Faculty Publications

Department of Respiratory Therapy

2015

Performance Comparisons of Jet and Mesh Nebulizers Using Different Interfaces in Simulated Spontaneously Breathing Adults and Children

Arzu Ari

Georgia State University, aari1@gsu.edu

Armèle Dornelas de Andrade

Universidade Federal de Pernambuco, armeledornelas@hotmail.com

Meryl M. Sheard

Georgia State University, Meryl@gsu.edu

Bshayer R. Alhamad

balhamad1@hotmail.com

James B. Fink

Georgia State University, jfink@gsu.edu

Follow this and additional works at: https://scholarworks.gsu.edu/rt_facpub

 Part of the [Respiratory System Commons](#)

Recommended Citation

Ari Arzu, Dornelas de Andrade Armele, Sheard Meryl, AlHamad Bshayer, and Fink James B.. Journal of Aerosol Medicine and Pulmonary Drug Delivery. -Not available-, ahead of print. doi:10.1089/jamp.2014.1149

This Article is brought to you for free and open access by the Department of Respiratory Therapy at ScholarWorks @ Georgia State University. It has been accepted for inclusion in Respiratory Therapy Faculty Publications by an authorized administrator of ScholarWorks @ Georgia State University. For more information, please contact scholarworks@gsu.edu.

Performance Comparisons of Jet and Mesh Nebulizers Using Different Interfaces in Simulated Spontaneously Breathing Adults and Children

Arzu Ari, PhD, RRT, PT, CPFT, FAARC¹, Armele Dornelas de Andrade, PhD, PT,² Meryl Sheard, MS, RRT¹, Bshayer AlHamad, MS¹, and James B. Fink, PhD, RRT, FAARC, FCCP¹

Abstract

Background: Different types of nebulizers and interfaces are used for the treatment of adults and children with pulmonary diseases. The purpose of this study was to determine the efficiency of a mesh nebulizer (MN) with a proprietary adapter and a jet nebulizer (JN) under different configurations in adult and pediatric models of spontaneous breathing. We hypothesize that delivery efficiency of JN and MN will differ depending on the interface used during aerosol therapy in simulated spontaneously breathing adult and pediatric models. While we expect that aerosol delivery with JN will be less efficient than MN, we also hypothesize that lung deposition obtained with the adult lung model will be more than that with the pediatric lung model in all conditions tested in this study.

Methods: A lung model using a teaching manikin connected to a sinusoidal pump via a collecting filter at the level of the bronchi simulating a spontaneously breathing adult (Vt 500 mL, RR 15 bpm, I:E ratio 1:2) or pediatric patient (Vt 150 mL, RR 25 bpm, I:E ratio 1:2). Albuterol sulfate (2.5 mg/3 mL) was aerosolized with JN (Mistymax 10, Airlife) or MN (Aerogen Solo[®], Aerogen) with the Adapter (Aerogen Solo[®] Adapter, Aerogen Ltd, Galway, Ireland) using mouthpiece, aerosol mask, and valved-mask in adults and the dragon mask, aerosol mask, and valved-mask in pediatrics ($n=3$). The Adapter, specifically designed for MN, was attached to all the interfaces used in this study with supplemental oxygen of 2 lpm, and in addition, the MP was tested with no additional flow in the adult model. The JN was driven with 10 lpm based on the manufacturer's label. Drug was eluted from the filter and analyzed via spectrophotometry. Descriptive statistics, dependent t -test and one-way analysis of variance were used for data analysis. Significant level was set at 0.05.

Results: In adults, delivery efficiency of JN with the valved mask was significantly greater than that with the aerosol mask ($p=0.01$). Aerosol delivery of JN with the mouthpiece was not statistically significant from the valved mask ($p=0.123$) and the aerosol mask ($p=0.193$). Drug delivery with MN with mouthpiece ($15.42 \pm 1.4\%$) and valved-mask ($15.15 \pm 1.1\%$) was greater than the open aerosol mask ($7.54 \pm 0.39\%$; $p=0.0001$) in the adult lung model. With no flow mouthpiece delivery increased > 2 fold ($34.9 \pm 3.1\%$; $p=.0001$) compared to use of 2 lpm of flow. Using the JN with the pediatric model deposition with valved-mask ($5.3 \pm 0.8\%$), dragon mask ($4.7 \pm 0.9\%$), and aerosol mask ($4.1 \pm 0.3\%$) were similar ($p>0.05$); while drug delivery with MN via valved-mask ($11.1 \pm 0.7\%$) was greater than the dragon mask ($6.44 \pm 0.3\%$; $p=0.002$) and aerosol mask ($4.6 \pm 0.4\%$; $p=0.002$), and the dragon mask was more efficient than the open aerosol mask ($p=0.009$).

Conclusion: The type of nebulizer and interface used for aerosol therapy affects delivery efficiency in these simulated spontaneously breathing adult and pediatric models. Drug delivery was greatest with the valved-mouthpiece and mask with JN and MN, while the standard aerosol mask was least efficient in these simulated spontaneously breathing adult and pediatric lung models. Delivery efficiency of JN was less than MN in all conditions tested in this study except in the aerosol mask. Lung deposition obtained with the adult lung model was more than that with the pediatric lung model.

Key words: adults, aerosols, drug delivery, face mask, inhalation therapy, mouthpiece, nebulizers, pediatrics

¹Department of Respiratory Therapy, Georgia State University, Atlanta, Georgia.

²Department of Physical Therapy, University Federal of Pernambuco, Recife, Brazil.

Introduction

AEROSOL THERAPY IS A WELL-ESTABLISHED method in the treatment of adults and children with pulmonary diseases. Recent advances in aerosol medicine led to the development of different types of nebulizers used for aerosol therapy. Jet nebulizers (JN) are commonly used in hospitals because of their inexpensive and easy to use nature. However, they require a compressor or pressurized gas source to operate, and tend to be inefficient, leaving up to 1.4 mL of medication in the reservoir at end of dose.⁽¹⁻⁴⁾ To overcome the limitations of JNs, several new nebulizer technologies, such as mesh nebulizers (MN), have been developed. The MN is electronically operated, requiring no gas to generate aerosol, with greater efficiency associated with low residual drug volume at end of nebulization (<0.1 mL).⁽⁴⁻⁷⁾

Both JN and MN are used for the treatment of adults and children with pulmonary diseases. However, it is well known that airway size, breathing pattern, inspiratory flow, and tidal volume change with age and affect drug delivery to the lung.^(2,8-11) Pulmonary deposition is higher in adults than in pediatrics because of an increase in lung volume, airway diameters, and inspiratory flow, as well as the development of a consistent breathing pattern, physical and cognitive abilities in adults. Evidence on delivery efficiencies of JN and MN using different interfaces in adults and pediatrics has been limited.

There are a variety of interfaces used in aerosol therapy, independent of the type of aerosol generator used. While mouthpiece and face mask are used for the delivery of aerosolized medications to adults, patients less than 3 years of age may not be able to hold and seal the mouthpiece between their lips reliably during aerosol therapy. Therefore, a face mask is commonly used in the treatment of pediatrics. However, it must be noted that use of a face mask with pediatrics is a substantial challenge. Previous studies emphasized the importance of a good face mask seal and reported that the face mask was not tolerated by children

during aerosol therapy.⁽¹²⁻²⁰⁾ Also, the practice of blow-by, directing the stream of aerosol to the face of a child has been associated with reduced delivery compared to a tightly fitting mask, with variable deposition associated with nebulizer type.⁽²¹⁾

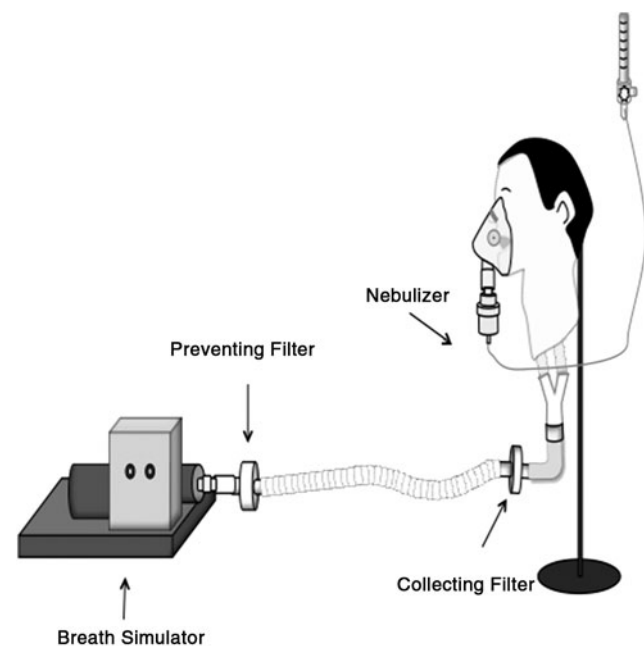
Although nebulizers are well-established devices in aerosol medicine, there are different types of nebulizers and interfaces used for aerosol therapy that raise some practical questions among clinicians in the treatment of adults and pediatrics with pulmonary diseases. These questions include: what is the efficiency of different nebulizers in spontaneously breathing patients when they are used based on the manufacturers' recommendations? How does the performance of a JN compare to MN using different interfaces in terms of drug delivery? and Is there any difference between their use in adults and children? The purpose of this study was to determine both the efficiency of the MN with an adapter specifically designed to facilitate aerosol therapy with or without low flow oxygen to spontaneously breathing nonintubated patients and JN using different interfaces in adult and pediatric models. We hypothesize that delivery efficiency of JN and MN will differ depending on the interface used during aerosol therapy in simulated spontaneously breathing adult and pediatric models. While we expect that aerosol delivery with JN will be less efficient than MN, we also hypothesize that lung deposition obtained with the adult lung model will be more than that with the pediatric lung model in all conditions tested in this study.

Methods

Lung model

As shown in Figure 1, a model using both adult and pediatric teaching mannequins with anatomical face and upper airways was connected via a collecting filter at the level of the bronchi to a sinusoidal pump simulating spontaneously breathing patterns for adult (V_t 500 mL, RR 15 bpm, I:E ratio 1:2) and pediatric (V_t 150 mL, RR 25 bpm, I:E ratio

FIG. 1. Experimental set-up of the adult or pediatric lung models used in this study.



1:2). A preventing filter was used to protect the sinusoidal pump from aerosols. A Y and elbow adapter were placed between the mainstem bronchi of the model and the collecting filter in order to prevent condensate or liquid medication from reaching the filter media (Fig. 1).

Nebulizers

JN (Mistymax 10, Airlife, Carefusion, Yorba Linda CA) and MN (Aerogen Solo[®], Aerogen Ltd, Galway, Ireland) with an Adapter (Aerogen Solo[®] Adapter, Aerogen Ltd) were tested in both the adult and pediatric models with all interfaces. Mistymax 10 is a single patient-use disposable conventional jet nebulizer that continuously nebulizes the medication, regardless of whether the patient is inhaling or exhaling. The JN was operated at 10 lpm in accordance with the manufacturer’s guidelines. The Aerogen Solo[®] is an electronically driven single patient-use aerosol generator that utilizes a vibrating mesh, where energy applied to the vibrational element, causes vibration of the 1000 tapered apertures within the mesh pumping liquid through the holes. MN was used with the Aerogen Solo[®] Adapter (Fig. 2) which allows administration of low flow oxygen during aerosol administration with mask and mouthpiece. The MN adapter has been approved for use in the European Union and the United States. The MN and adapter were operated with supplemental oxygen of 2 lpm with all interfaces, and no flow with the valved mouthpiece.

Interfaces

Figure 3 represents the organizational scheme of the study. With the adult model, the valved mouthpiece, open aerosol mask (AirLife[®], Carefusion, San Diego, CA) and valved-mask (AirLife) were used with both aerosol devices. When JN was used with a mouthpiece in the adult lung model, a t-piece attached to the nebulizer was configured with a mouthpiece

on patient side with a 6 inch 22mm extension tube as reservoir on the other side. As pediatrics may not reliably use a mouthpiece, the dragon mask (AirLife), open pediatric aerosol mask (AirLife) and valved-mask (AirLife) were tested with the pediatric model (Fig. 4). The valved-mask was a modifying a non-rebreathing oxygen mask so that gas passes from the mask through the one-way valves on exhalation, while limiting gas entry through the valves during inspiration. All experiments were conducted under ideal conditions in which each nebulizer and interface effectively sealed to the face of the teaching mannequins to ensure the absence of potential facemask or mouthpiece leak.

Dosage

Albuterol sulfate (2.5 mg) in a total volume 3 mL was nebulized with both nebulizers in all runs. All nebulizers were operated in accordance with the manufacturer’s recommendations and ran until nebulization ended.

Data collection

Aerosol drug delivered to an absolute filter positioned distal to the mannequin’s mainstem bronchi was eluted with 0.1 molar N hydrochloric acid for 3 min with gentle agitation, and measured using a spectrophotometer (Beckman Instruments, Fullerton, California), at a wavelength of 276 nm. The amount of drug was quantified and expressed as a percentage of the original dose delivered. The experiment was repeated three times (n=3) for each nebulizer in both adults and pediatrics.

Data analysis

The amount of drug depositing in the filter was expressed as mg of drug, as well as the total fraction of the nominal dose

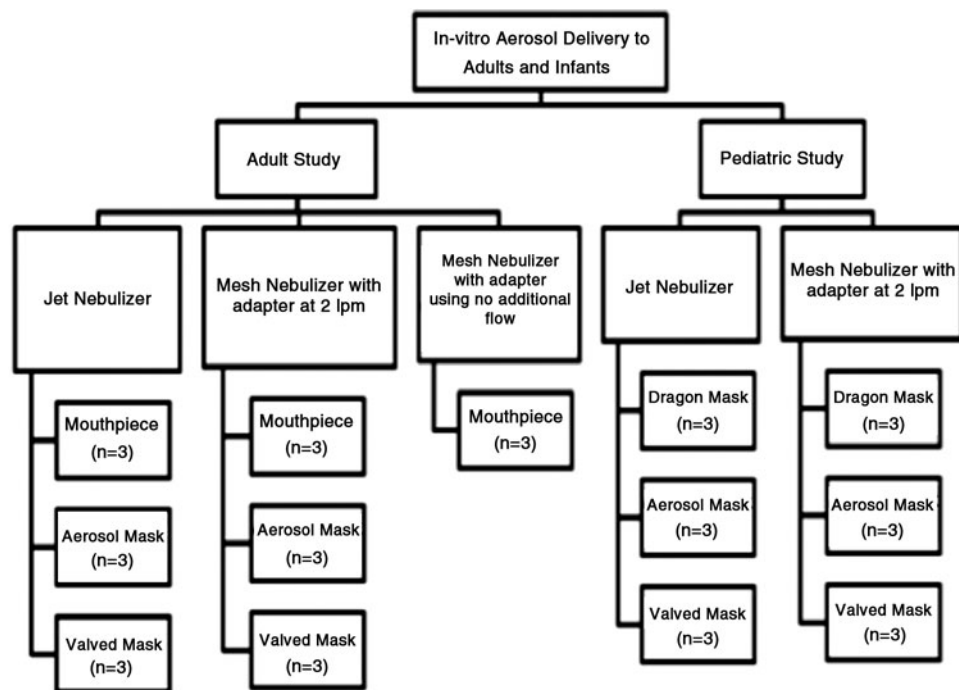
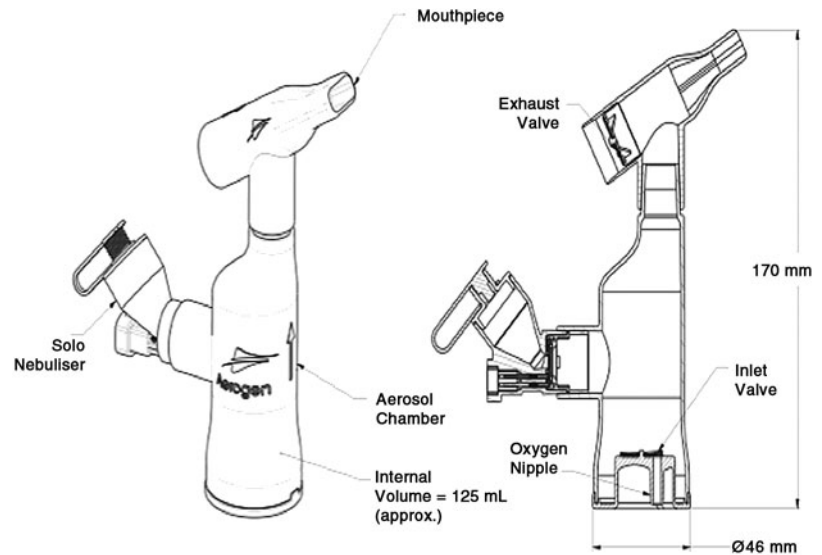


FIG. 2. Organizational scheme of the study.

FIG. 3. Schematic illustration of the Aerogen Solo Adapter. The adapter chamber is 170 mm by 46 mm, with an internal volume of 125 mL. A one-way flap valve is placed on the chamber inlet, and covers the oxygen nipple to avoid leakage when no oxygen is being introduced. The mouthpiece has a one-way expiratory flap valve.



placed in each nebulizer. Descriptive statistics including the mean and standard deviations were calculated for total inhaled mass and total inhaled mass percent. Differences in means between inhaled mass percent for the three interfaces used in the adult and pediatric models were compared with a one-way analysis of variance were used for data analysis. The Scheffé procedure was employed for post-hoc comparisons of the interfaces tested in this study. The dependent *t*-test was used to determine differences in inhaled drug mass percent between JN and MN using each interface in each lung model. Significant level was set at 0.05.

Results

Delivery efficiency of each nebulizer using different interfaces

Table 1 shows mean \pm SD for inhaled mass and percentage of nominal dose delivered distal to the bronchi of the adult lung model. In adults, delivery efficiency of JN with

the valved mask was significantly higher than that with the aerosol mask ($p=0.01$). Aerosol delivery of JN with the mouthpiece was not statistically different from the valved-mask ($p=0.123$) and the aerosol mask ($p=0.193$) using the adult lung model. Drug delivery with MN with mouthpiece ($15.42 \pm 1.4\%$) and valved-mask ($15.15 \pm 1.1\%$) was greater than the open aerosol mask ($7.54 \pm 0.39\%$; $p=0.0001$). With no flow mouthpiece delivery increased >2 fold ($34.9 \pm 3.1\%$; $p=0.0001$) compared to use of 2 lpm of flow.

Table 2 shows mean \pm SD for inhaled mass and percentage of nominal dose delivered distal to the bronchi of the pediatric lung model. Using the JN with the pediatric model deposition with valved-mask ($5.3 \pm 0.8\%$), dragon mask ($4.7 \pm 0.9\%$), and aerosol mask ($4.1 \pm 0.3\%$) were similar ($p>0.05$); while drug delivery with MN via valved-mask ($11.1 \pm 0.7\%$) was greater than the dragon mask ($6.44 \pm 0.3\%$; $p=0.002$) and aerosol mask ($4.6 \pm 0.4\%$; $p=0.002$), and the dragon mask was more efficient than the open aerosol mask ($p=0.009$).

FIG. 4. Types of interfaces tested with the adult (*upper*) and pediatric models. In the *upper panel*, adult interface from *left to right* include JN with MP and 6 inch 22 mmID corrugated tubing as reservoir, JN with open aerosol mask, MN with adapter and valved mask, and MN with MP. In the *lower panel*, pediatric interfaces include open aerosol mask, MN with adapter and dragon mask, and JN with valved mask.

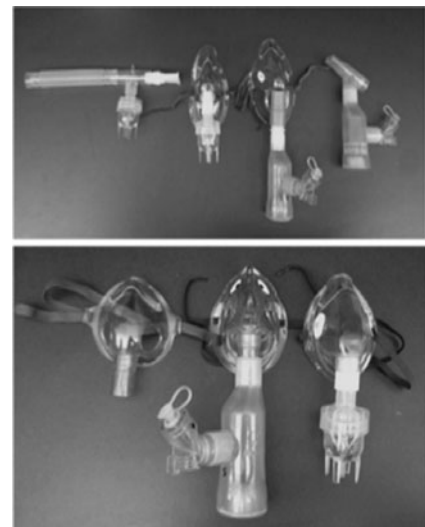


TABLE 1. MEAN \pm SD FOR INHALED MASS AND PERCENTAGE OF NOMINAL DOSE DELIVERED DISTAL TO BRONCHI OF ADULT LUNG MODEL

Nebulizers	Jet nebulizer			Mesh nebulizer at 2 lpm			Mesh nebulizer using no O ₂ Mouthpiece
	Mouthpiece	Valved mask	Aerosol mask	Mouthpiece	Valved mask	Aerosol mask	
Inhaled mass (mg)	0.19 \pm 0.01	0.22 \pm 0.01	0.17 \pm 0.01	0.39 \pm 0.03	0.38 \pm 0.02	0.188 \pm 0.01	0.87 \pm 0.07
Inhaled mass percent (%)	7.66 \pm 0.62	8.63 \pm 0.22	6.84 \pm 0.49	15.42 \pm 1.41	15.15 \pm 1.05	7.54 \pm 0.39	34.99 \pm 3.17

Jet nebulizer versus mesh nebulizer

As shown in Table 1, delivery efficiency of JN was two-fold less than MN when a mouthpiece or valved-mask ($p=0.014$ and $p=0.013$, respectively) was used for aerosol therapy using the adult lung model. While drug delivery with MN attached to an open aerosol mask was significantly less efficient than mouthpiece and valved-mask ($p=0.0001$ and $p=0.0001$, respectively), aerosol deposition obtained from mouthpiece and valved-mask showed no significant difference using JN and MN ($p=0.121$ and $p=0.951$, respectively). Without supplemental O₂, MN with mouthpiece achieved >4 fold higher deposition efficiency than JN with MP used with the adult lung model.

JN was less efficient in drug delivery than MN using valved-mask and trended lower with the dragon mask ($p=0.002$ and $p=0.066$, respectively). Differences in aerosol delivery between JN and MN using the open aerosol mask was not statistically significant ($p=0.355$). While no significant difference was found between valved-mask, dragon mask, and aerosol mask using JN, drug delivery with MN via valved-mask was greater than the dragon mask ($p=0.002$) and open aerosol mask ($p=0.002$). The dragon mask was more efficient than the aerosol mask using MN ($p=0.009$).

Also, inhaled dose distal to the bronchi was marginally greater with adults than peds with all of the masks studied with both JN and MN ($p<0.05$).

Adult versus Infant

Aerosol deposition in the adult lung model was significantly greater than the infant lung model using aerosol and valved masks with JN ($p=0.001$, and $p=0.002$, respectively) and MN ($p=0.001$, and $p=0.005$, respectively). Figure 5 shows comparisons of adult and infant lung model on aerosol delivery using aerosol and valved-masks with JN and MN.

Discussion

Aerosol therapy via nebulizers is a well-established method for treatment of patients with pulmonary diseases.

However, no consensus exists on which nebulizer to use with which interface in adults and pediatrics. In this study, we showed that performance of nebulizers varies with the nebulizer type and interface used during aerosol therapy. Delivery efficiency of JN was less than MN in all conditions tested in this study, except in the aerosol mask in simulated spontaneously breathing adult and pediatric lung models. Regardless of the type of nebulizer, drug delivery via the open aerosol mask was less than other interfaces tested with both adult and pediatric models. In the pediatric model, aerosol deposition obtained via the valved-mask was greater than the dragon and open aerosol. With each type of nebulizer, delivery with mouthpiece and the valved-mask were similar.

One of the advantages of MN, generating aerosol without requirements for oxygen or other gas flow to generate aerosol, can be a disadvantage in patients requiring low flow oxygen during nebulization. Unlike a JN that is typically operated at a specific flow with oxygen or air, the MN adapter allows low flow oxygen to be titrated based on patient needs, independent of the performance parameters of the nebulizer, without requiring use of a blender.

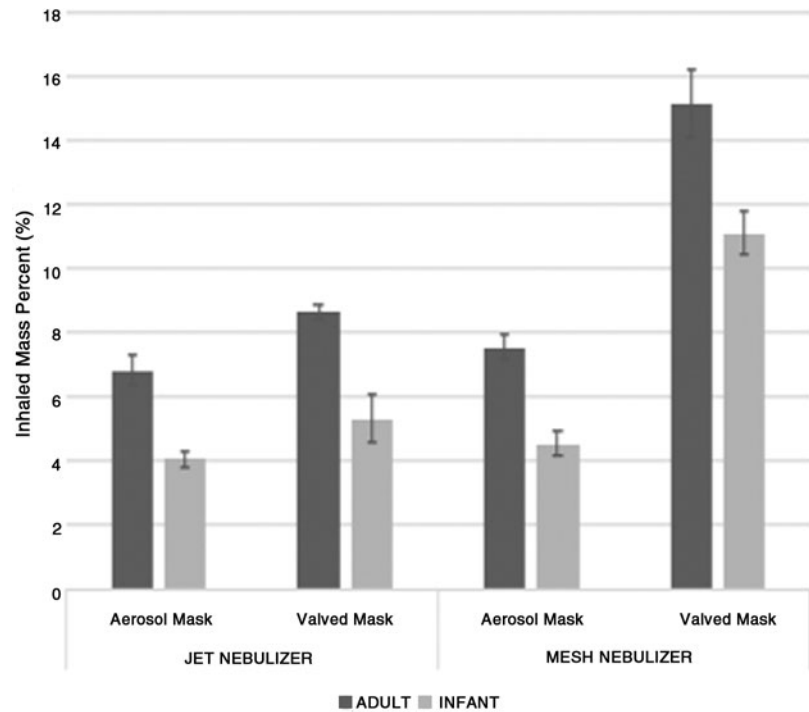
The adapter was designed with a valved mouthpiece to facilitate administration of low flow oxygen with a valved chamber to optimize aerosol delivery. Valved holding chambers (VHC) with valved masks and mouthpieces have been used with aerosol devices, specifically pMDIs, for several decades, increasing inhaled dose compared to pMDIs alone.⁽²²⁾ But similar to pMDI with VHC and jet nebulizers administered to children with masks, failure to have a tight seal substantially reduces inhaled aerosol.^(17,23,24) Similarly, open ports on the aerosol mask was associated with a reduction of inhaled dose with both the open and dragon masks compared to the valved mouthpiece or mask.

Aerosols can be administered via either mouthpiece or face mask. Nikander et al.⁽²⁵⁾ reported that the inhaled mass percent of a jet nebulizer attached to a mouthpiece ranges from 8.9% to 12.2%, as opposed to 5.0%–6.9% with a standard nonsealed face mask. Consistent with Nikander's

TABLE 2. MEAN \pm SD FOR INHALED MASS AND PERCENTAGE OF NOMINAL DOSE DELIVERED DISTAL TO BRONCHI OF PEDIATRIC LUNG MODEL

Nebulizers	Jet nebulizer			Mesh nebulizer		
	Valved mask	Dragon mask	Aerosol mask	Valved mask	Dragon mask	Aerosol mask
Inhaled mass (mg)	0.13 \pm 0.02	0.116 \pm 0.02	0.10 \pm 0.01	0.277 \pm 0.01	0.161 \pm 0.01	0.11 \pm 0.01
Inhaled mass %	5.33 \pm 0.75	4.67 \pm 0.94	4.08 \pm 0.27	11.11 \pm 0.66	6.44 \pm 0.34	4.56 \pm 0.37

FIG. 5. Comparison of adult (dark bar) and infant (gray bar) inhaled mass percent (Mean \pm SD) for open and valved aerosol mask with jet and mesh nebulizers. Inhaled mass was greater with adult than infant with all conditions ($p < 0.05$).



study, we found aerosol deposition obtained via an open face mask was lower than mouthpiece (6.84% and 7.66%, respectively). Differences in magnitude between the mouthpiece and face mask may be the characteristics of the aerosol devices with the drug nebulized. Budesonide is associated with a higher particle size distribution than albuterol that we used, which may preferentially increase impactive losses for aerosol passing through the nasal passages of the model.

There are a few studies that compared clinical efficacy of the face mask with the mouthpiece. For instance, Mellon et al.⁽²⁶⁾ found that the open face mask was as effective as the mouthpiece in delivering budesonide inhalation suspension to young children with persistent asthma. In contrast, Kishida et al.⁽²⁷⁾ reported that aerosol delivery via mouthpiece leads to significant improvement in forced expiratory volume in the first second (FEV₁) compared to face mask. On the other hand, Everard et al.⁽²⁸⁾ reported approximately 50% decrease in aerosol deposition in the lungs with nasal inhalation, which is an option with mask that is excluded with use of mouthpiece.

Although it appears to be more efficient to use a mouthpiece with nebulizers, sick, acutely dyspneic and uncooperative adults and children less than 3 years of age may not be able to use a mouthpiece reliably during aerosol therapy. In such cases, nebulizers are often used with face masks. When a face mask is used during aerosol therapy, it is essential to have a tight seal between face and mask in order to avoid aerosol leakage and aerosol deposition around the eyes.^(16,24)

There are different types of face masks available on the market for aerosol therapy. While we tested the standard open aerosol mask with the dragon and valved-mask in the pediatric study, only the standard face mask and valved-face mask were compared in the adult study. Like Lin et al.,⁽²⁹⁾

we found an increased efficiency with the valved-face mask than the standard aerosol mask. The valved-mask contains one-way valves on both sides of the mask that allows exhaled gas to exit the mask, while providing a preferential draw of aerosol and gas from the aerosol generator/adaptor during inhalation that resulted in increased aerosol deposition in these simulated spontaneously breathing adult and pediatric models. Restrepo et al.³⁰ determined the amount of aerosol delivered to a pediatric lung model via T-piece and an aerosol mask at 0 cm, 1 cm, and 2 cm away from the filter. The mean inhaled mass percent measured with the aerosol mask at 0 cm was 2.88% as opposed to 4.08% in our study. Restrepo et al.³⁰ used a set tidal volume of 60 ml and a respiratory rate of 20 bpm whereas we used a set tidal volume of 150 ml and a respiratory rate of 25 bpm. Differences in breathing parameters may be the major source of the differences in our findings. Similarly, Lin et al. investigated the effect of the dragon, aerosol, and fish masks on aerosol deposition at three different distances (0 cm, 1 cm, and 2 cm) from the face of a pediatric breathing model, with a mean percentage of nominal dose inhaled of 2.18% and 2.65% with the aerosol mask and the dragon mask, respectively.³¹ Lin also used the same breathing parameters as Restrepo et al.

Although the valved mask is a nonstandard configuration, our results suggest that the valved mask substantially increased the inhaled dose with both types of aerosol generator. However, failure to have a tight seal, as we were careful to achieve with our models, would likely result in a substantial reduction of inhaled drug available to the patient. Pitance and colleagues⁽³²⁾ reported that both inhaled and lung dose were greater with a nonvented nebulizer using a corrugated extension tube reservoir than use of a vented nebulizer. While these extensions are commonly used with JN with mouthpiece, we were surprised to find that the valved mask

delivered a similar level of inhaled dose, suggesting that the volume of the mask acts as a reservoir of aerosol.

This study confirms high efficiency of aerosol delivery with mesh nebulizers compared to jet nebulizers in simulated spontaneously breathing patients. In the current study, drug delivery with MN increased by up to 2-fold both in adults and pediatrics with a flow of 2 lpm. The 2-fold increase with valved mask is likely clinically significant. With the MN and Adapter, we found a 35% greater inhaled dose with the Dragon ($6.44 \pm 0.34\%$) versus open aerosol mask ($4.56 \pm 0.37\%$). Nonetheless, clinicians should be cautious in implying that such an increase is clinically significant in real life situations, particularly when there are no data about the mask seal.

We speculate that the increased inspiratory resistance through the smaller ports with the dragon mask versus open aerosol mask allows a greater percentage of inhaled gas to be drawn through the adapter. However, Berlinski⁽³³⁾ compared inhaled dose from JN with open aerosol masks with various level of occlusion of the ports and reported no difference.

More than a 4-fold increase in drug delivery was observed with the MN using MP in the adult lung model with no oxygen flow. This is consistent with reports of higher efficiency with MN than JN during mechanical ventilation,^(34–36) and with a mouthpiece.⁽³⁷⁾ Nebulizers that employ mesh technology have a low residual volume, silent operation, short treatment time, simplified cleaning, and the ability to nebulize small drug volumes.^(2,4,37–40)

We found that using 2 lpm with the MN attached to a mouthpiece decreased drug delivery compared to no oxygen flow. This is likely due to the continuous flow of gas diluting the aerosol and displacing it from the relatively small volume spacer chamber. This is consistent with previous reports that increasing bias flow leads to a dilutive effect with a trend toward a reduction in drug delivered to adults during mechanical ventilation in which the ventilator circuit acts as a reservoir.⁽³⁵⁾ In contrast, with no gas flow into the adapter, aerosol does not effectively enter the open mask. Based on our observations and the device label, MN with open aerosol mask requires some level of low flow gas through the adapter to move the aerosol from the chamber into the mask.

Despite technological advances in nebulizer designs, jet nebulizers are still extensively employed to deliver inhaled medications to patients with pulmonary diseases. This is in part due to the low costs associated with jet nebulizers, and the relatively high cost of the mesh technology, especially when administering drugs that are inexpensive such as bronchodilators. The main problem with these nebulizers is the continuous aerosol generation both in inhalation and exhalation that leads to inefficiency in aerosol drug delivery and substantial drug loss into the environment.^(2,6,41) According to *in vitro* reports by Rau et al.,⁽⁴²⁾ the inhaled dose obtained from a jet nebulizer is 14% using a simulated adult lung model. Their results are in contrast to the findings of this study, as we found that aerosol drug delivery with JN is 6.84%, 7.66%, and 8.63% using the aerosol mask, mouthpiece, and valved-mask, respectively. Differences in our findings can be explained by the models used as Rau et al. collected the inhaled dose at the face, as opposed to our model that collected the inhaled drug distal to the bronchi. Since our model allows aerosol to pass through the anatomic structures of the upper airway, the inhaled dose available to the lung would be reduced due to impactive losses of aerosols

in the upper airway. Also, aerosols inhaled during the last 25% of inhalation are less likely to reach the filter attached to the trachea. The findings of the pediatric study showed that aerosol deposition with JN ranged from 4.08% to 5.33%, which is consistent with the results of an *in vivo* study conducted by Erzinger et al. on 18–36-month-old children.⁽²⁴⁾

We found only marginal increases in the inhaled dose with adults over pediatrics with the range of masks used. The differences in airway sizes and volumes are in part offset by the similar I:E ratios used with both models.

Limitations

This study used one set of breathing parameters for each model; therefore, the findings of this study should not be generalized to the wide range of breathing parameters representing different age ranges of children and sizes of adults. Although it is well known that children usually have highly erratic breathing patterns while awake which impacts deposition, and this is further exacerbated by their intolerance of the face mask, mimicking such changes in breathing pattern or the failure to tolerate a closely fitting face mask was beyond the scope of this study. Since our model provides a very consistent flow, volume, and frequency during aerosol treatment, the findings of this study may overestimate aerosol drug delivery *in vivo*.

The use of valved disposable face masks is not as common in aerosol delivery as in administration of oxygen or heliox. We used these masks to better understand their impact on inhaled mass with our models. While our findings of improved inhaled dose are compelling, our evaluation does not include the impact on CO₂ rebreathing or other potential safety concerns with their use. Further modeling and evaluation is recommended to determine their safety in the clinical settings.

Also, the MN adapter is new to the market and approved for use by the EU and FDA. Therefore the clinical experience to date is limited, with no clinical studies to date.

Clinical implications

Clinicians often question the effectiveness of nebulizers that are used with different interfaces. In this study, we compared the use of JN and MN with three types of interfaces in simulated spontaneously breathing adults and pediatrics. The data indicated that MN was superior to JN in terms of aerosol drug delivery, and aerosol deposition obtained with the valved-mouth pieces and face mask was greatest, regardless of the nebulizer tested in this study. Efficiency of MN attached to a mouthpiece is better when no additional flow was used with the Adapter than 2 lpm. Further studies are needed in the clinical settings to determine the clinical efficacy of higher doses and their impact on patients safety, outcomes and resource utilization.

Conclusion

The type of nebulizer and interface used for aerosol therapy affected delivery efficiency in these simulated spontaneously breathing adult and pediatric lung models. Drug delivery was greatest with the valved-mouthpiece and valved-mask with both JN and MN, while the standard aerosol mask was least efficient in these simulated spontaneously breathing

adult and pediatric lung models. Delivery efficiency of JN was less than MN in all conditions tested in this study except with the open aerosol mask. Lung deposition obtained with the adult lung model was more than that with the pediatric lung model.

Acknowledgments

This study was funded by an unrestricted research grant provided by Aerogen Ltd.

Author Disclosure Statement

Dr. Ari, Dr. Dornelas, Mr. Harwood, Ms. AlHamad, and Ms. Sheard have no conflict of interest with regard to this paper. Dr. Fink is a consultant for the biotech industry whose clients include Aerogen, Ltd., Dance Biopharm, Parion, Bayer, Quark, and Aridis.

References

- Ari A, Hess D, Myers TR, and Rau JL: *A Guide to Aerosol Delivery Devices for Respiratory Therapists*. Dallas, Texas: Am Assoc Respir Care; 2009.
- Ari A, and Fink J: Guidelines to aerosol devices in infants, children and adults: Which to choose, why and how to achieve effective aerosol therapy? *Expert Rev Respir Med*. 2011;5:561–572.
- Ari A, and Fink J: Aerosol therapy in children: Challenges and solutions. *Expert Rev Respir Med*. 2013;7:665–672.
- Dolovich MB, and Dhand R: Aerosol drug delivery: Developments in device design and clinical use. *Lancet*. 2010;377:1032–1045.
- Dhand R: Nebulizers that use a vibrating mesh or plate with multiple apertures to generate aerosol. *Respir Care*. 2002;47:1406–1416.
- Hess DR: Aerosol delivery devices in the treatment of asthma. *Respir Care*. 2008;53:699–723.
- Waldrep JC, and Dhand R: Advanced nebulizer designs employing vibrating mesh/aperture plate technologies for aerosol generation. *Curr Drug Deliv*. 2008;5:114–119.
- Pongracic JA: Asthma delivery devices: Age-appropriate use. *Pediatr Ann*. 2003;32:50–54.
- Devadason SG, and Le Souef PN: Age-associated factors influencing the efficacy of various forms of aerosol therapy. *J Aerosol Med*. 2002;15:343–345.
- Everard ML: Aerosol delivery to children. *Pediatr Ann*. 2006;35:630–636.
- Everard ML: Inhalation therapy for infants. *Adv Drug Deliv Rev*. 2003;55:869–878.
- Amirav I, and Newhouse MT: Aerosol therapy with valved holding chambers in young children: Importance of the facemask seal. *Pediatrics*. 2001;108:389.
- Esposito-Festen JE, Ates B, van Vliet FJ, Verbraak AF, de Jongste JC, and Tiddens HA: Effect of a facemask leak on aerosol delivery from a pMDI-spacer system. *J Aerosol Med*. 2004;17:1–6.
- Smaldone GC: Assessing new technologies: Patient-device interactions and deposition. *Respir Care*. 2005;50:1151–1160.
- Smaldone GC, Sangwan S, and Shah A: Facemask design, facial deposition, and delivered dose of nebulized aerosols. *J Aerosol Med*. 2007;20:S66–75.
- Hayden J, Smith N, Woolf D, Barry P, and O’Callaghan C: A randomised crossover trial of facemask efficacy. *Arch Dis Child*. 2004;89:72–73.
- Nikander K, Berg E, and Smaldone GC: Jet nebulizers versus pressurized metered dose inhalers with valved holding chambers: Effects of the facemask on aerosol delivery. *J Aerosol Med*. 2007;20:S46–55.
- Janssens HM, and Tiddens HA: Facemasks and aerosol delivery by metered dose inhaler-valved holding chamber in young children: A tight seal makes the difference. *J Aerosol Med*. 2007;20:S59–63.
- Esposito-Festen J, Ates B, van Vliet F, Hop W, and Tiddens H: Aerosol delivery to young children by pMDI-spacer: Is facemask design important? *Pediatr Allergy Immunol*. 2005;16:348–353.
- Amirav I, and Newhouse MT: Review of optimal characteristics of face-masks for valved-holding chambers (VHCs). *Pediatr Pulmonol*. 2008;43:268–274.
- Mansour MM, and Smaldone GC: Blow-by as potential therapy for uncooperative children: An in-vitro study. *Respir Care*. 2012;57:2004–2011.
- Zac M, Madson J, and Berg E: A mathematical model of aerosol holding chambers. *J Aerosol Med*. 1999;12:187–196.
- Smaldone GC, Berg E, and Nikander K: Variation in pediatric aerosol delivery: Importance of facemask. *J Aerosol Med*. 2005;18:354–363.
- Erzinger S, Schuepp KG, Brooks-Wildhaber J, Devadason SG, and Wildhaber JH: Facemasks and aerosol delivery in vivo. *J Aerosol Med*. 2007;20:S78–83.
- Nikander K, Agertoft L, and Pedersen S: Breath-synchronized nebulization diminishes the impact of patient-device interfaces (face mask or mouthpiece) on the inhaled mass of nebulized budesonide. *J Asthma*. 2000;37:451–459.
- Mellon M, Leflein J, Walton-Bowen K, Criz-Rivera M, Fitzpatrick S, and Smith J: Comparable efficacy of administration with facemask or mouthpiece of nebulized budesonide inhalation suspension for infants and young children with persistent asthma. *Am J Respir Crit Care Med*. 2000;162:593–598.
- Kishida M, Suzuki I, Kabayama H, Koshibu T, Izawa M, Takeshita Y, Kurita F, Okada M, Shinomiya N, and Aoki T: Mouthpiece versus facemask for delivery of nebulized salbutamol in exacerbated childhood asthma. *J Asthma*. 2002;39:337.
- Everard ML, Hardy JG, and Milner AD: Comparison of nebulised aerosol deposition in the lungs of healthy adults following oral and nasal inhalation. *Thorax*. 1993;48:1045–1046.
- Lin HL, Wan GH, Chen YH, Fink JB, Liu WQ, and Liu KY: Influence of nebulizer type with different pediatric aerosol masks on drug deposition in a model of a spontaneously breathing small child. *Respir Care*. 2012;57:1894–1900.
- Restrepo RD, Dickson SK, Rau JL, and Gardenhire DS: An investigation of nebulized bronchodilator delivery using a pediatric lung model of spontaneous breathing. *Respir Care*. 2006;51:56–61.
- Lin HL, Restrepo RD, Gardenhire DS, and Rau JL: Effect of face mask design on inhaled mass of nebulized albuterol, using a pediatric breathing model. *Respir Care*. 2007;52:1021–1026.
- Pitance L, Reyckler G, Leal T, Reyckler H, Liistro G, Montharu J, Diot P, and Vecellio L: Aerosol delivery to the lung is more efficient using an extension with a standard jet nebulizer than an open-vent jet nebulizer. *J Aerosol Med Pulm Drug Deliv*. 2013;26:208–214.

33. Berlinski A: Effect of mask dead space and occlusion of mask holes on delivery of nebulized albuterol. *Respir Care*. 2014;59:1228–1232.
34. Ari A, Areabi H, and Fink JB: Evaluation of position of aerosol device in two different ventilator circuits during mechanical ventilation. *Respir Care*. 2010;55:837–844.
35. Ari A, Atalay OT, Harwood R, Sheard MM, Aljamhan EA, and Fink JB: Influence of nebulizer type, position, and bias flow on aerosol drug delivery in simulated pediatric and adult lung models during mechanical ventilation. *Respir Care*. 2010;55:845–851.
36. Sidler-Moix A, Dolci U, Gryllaki M, Pannatier A, Cotting J, and Di Paolo ER: Albuterol delivery in an in vitro pediatric ventilator lung model: Comparison of jet, ultrasonic and mesh nebulizers. *Pediatric Crit Care Med*. 2013;14:1–5.
37. Johnson JC, Waldrep JC, Guo J, and Dhand R: Aerosol delivery of recombinant human DNase I: In vitro comparison of a vibrating-mesh nebulizer with a jet nebulizer. *Respir Care*. 2008;53:1703–1708.
38. Kurosaka F, and Nishio H: Comparison of the bronchodilative effects of salbutamol delivered via three mesh nebulizers in children with bronchial asthma. *Allergol Int*. 2009;58:529–535.
39. Rubin B: Pediatric aerosol therapy: New devices and new drugs. *Respir Care*. 2011;56:1411–1421.
40. Rubin BK: Air and soul: The science and application of aerosol therapy. *Respir Care*. 2010;55:911–921.
41. Rau JL: The inhalation of drugs: Advantages and problems. *Respir Care*. 2005;50:367–382.
42. Rau JL, Ari A, and Restrepo RD: Performance comparison of nebulizer designs: Constant-output, breath-enhanced, and dosimetric. *Respir Care*. 2004;49:174–179.

Received on April 16, 2014
in final form, October 4, 2014

Reviewed by:
Israel Amirav
Ariel Berlinski

Address correspondence to:
Dr. Arzu Ari
Division of Respiratory Therapy
Georgia State University
P.O. Box 4019
Georgia 30302-4019

E-mail: arzuari@hotmail.com