Influence of Nebulizer Type With Different Pediatric Aerosol Masks on Drug Deposition in a Model of a Spontaneously Breathing Small Child

Hui-Ling Lin MSc RRT RN FAARC, Gwo-Hwa Wan PhD, Yuan-Huey Chen MSc PT, James B Fink PhD RRT FAARC, Wen-Qie Liu RRT, and Kai-Ying Liu RRT

BACKGROUND: The performance of nebulizers varies with the design type as well as the breathing patterns of various age groups. The present study quantified aerosol delivery using spontaneously breathing parameters of a small child (2–4 years) by a lung simulator to determine the influence of nebulizer type, actuation mechanisms, and pediatric aerosol masks. METHODS: Three types of nebulizer (constant-output, breath-enhanced, and breath-actuated nebulizer) and 3 masks (standard pediatric mask, the Fish mask, and a valved mask) were chosen for the testing. The actuation mechanism of the breath-actuated nebulizer was tested by manual synchronization with inspiration, breath actuation, and continuous nebulization. The nebulizer performance was determined by determining mass median aerodynamic diameter and analyzing drug deposition distal to the trachea (inhaled mass), on the face, on the mask, residual drug in the nebulizer, and the time of nebulization. The quantity of salbutamol deposited was determined by spectrophotometry (276 nm). RESULTS: Mass median aerodynamic diameter was similar across nebulizers. Breath-actuated nebulization generated a lower inhaled dose and higher nebulization time than continuous nebulization ($P = .001$). Breath synchronized aerosol generation, whether breath-actuated or manually actuated, yielded 10–20 times lower inhaled mass than continuous nebulization (0.1–0.6% vs 5–11%, respectively). The AeroEclipse, operated continuously, delivered greater inhaled dose than the LC Plus ($P = .025$). Higher inhaled dose was achieved with the Fish mask than standard or valved mask, with all nebulizers tested ($P = .001$). CONCLUSIONS: In this model using ventilatory parameters associated with a 2–4-year-old child, breath-actuated nebulization was not as effective as continuous nebulization. Aerosol mask design can impact inhaled drug dose across the range of nebulizers tested. *Key words: pediatrics; aerosol therapy; jet nebulizer; constant-output nebulizer; breath-enhanced nebulizer; breath-actuated nebulizer; aerosol masks.* [Respir Care 2012;57(11):1894–1900. © 2012 Daedalus Enterprises]

Ms Lin, Dr Wan, and Ms Chen are affiliated with the Department of Respiratory Therapy, Chang Gung University, Taoyuan, Taiwan. Dr Fink is affiliated with the Division of Respiratory Therapy, Georgia State University, Atlanta, Georgia. Wen-Qie Liu is affiliated with the Department of Respiratory Therapy, Keelung Branch, Chang Gung Memorial Hospital, Keeling, Taiwan. Kai-Ying Liu is affiliated with the Department of Respiratory Therapy, Chang Gung Memorial Hospital, LinKou Branch, Linkou, Taiwan.

Hui-Ling Lin presented a version of this paper at the AARC Congress 2010, held December 6–8, 2010, in Las Vegas, Nevada.

Dr Fink has disclosed relationships with Aerogen, Dance Pharma, Kalobios, and Novartis. The other authors have disclosed no conflicts of interest.

Correspondence: Hui-Ling Lin MSc RRT FAARC, Department of Respiratory Therapy, Chang Gung University, 259 Wan-Hau First Road, Kwei-Shang, Taoyuan, Taiwan 33301. E-mail: huilingrrt@gmail.com.

DOI: 10.4187/respcare.01652

Introduction

Gas-powered jet nebulizers are commonly used for delivering medications to pediatric patients, due to their low cost and minimal technique requirements. However, numerous factors may affect drug deposition, such as the type of nebulizer, the interface between nebulizer and patient, and the patient's breathing pattern.[1-6] Face masks are commonly used accessories to nebulizers for delivering aerosolized medications to infants, toddlers, and preschool children. Applying aerosol treatments with a properly sized mask, firmly placed against the face, increases the inhaled drug amount, while drug deposition decreases when the distance of the mask from the face increases.[3,7,8] Changing the shape of the aerosol mask and angle of attachment to the nebulizer influences aerosol deposition.[3,6] Yet the influence of different pediatric mask designs when used with different types of nebulizers has not been well studied.

Jet nebulizer designs fall into 3 categories: constant-output, breath-enhanced, and breath-actuated. Of these, the breath-actuated nebulizer (BAN) has been described as providing superior efficiency in drug delivery, both in pediatrics and in adults.[6,9-13] The BAN, when adequately actuated by the patient's inspiratory effort, generates aerosol only during inspiration, reducing the waste of the drug during expiration. The manufacturer suggests that the BAN can be used with patients generating an inspiratory flow $\geq$ 15 L/min, and has designed a valved mask for use of the BAN with small children. When a patient fails to consistently breath-actuate the BAN, pressing a manual override button allows either continuous aerosol output or manually synchronized aerosol generation with the child's breathing pattern. The efficiency of aerosol delivery through a BAN with different masks and actuation mechanisms has not been compared with continuous nebulization from other types of jet nebulizers in small children. Therefore, the purpose of this in vitro study was to demonstrate the influence of continuous nebulization and different actuated mechanisms with a BAN across 3 designs of jet nebulizer when used with a variety of pediatric aerosol masks.

QUICK LOOK

Current knowledge

Gas-powered jet nebulizers are commonly used for aerosol delivery to pediatric patients, due to their low cost and minimal technique requirements. Numerous factors have been demonstrated to affect drug deposition, including the type of nebulizer, the interface, and breathing pattern.

What this paper contributes to our knowledge

In a pediatric model of the respiratory tract, a breath-actuated or manually breath-synchronized nebulizer delivered only a small fraction of the inhaled tracheal dose achieved with continuous aerosol generation. These findings require validation in a clinical trial.

Methods

This research was in part funded by the Ministry of Education, Republic of China, and was performed at Chang Gung University.

Lung Model

A lung simulator (ASL 5000, IngMar Medical, Pittsburg, Pennsylvania) was set to represent a spontaneously breathing child between 2–4 years of age with a tidal volume of 150 mL, inspiratory time 0.8 second, peak inspiratory flow 20 L/min, and respiratory rate 25 breath/min.[14,15] The face and anatomical upper airway of a cardiopulmonary resuscitation mannequin, representing a 2-year-old child (GD/CPR 150, Ying Sheng Scientific Apparatus, Taipei, Taiwan), were modified to attach a bacteria filter (Galemed, I-Lan, Taiwan) for the collection of inhaled aerosol particles distal to the trachea. A second filter was placed between the inspiratory filter and the lung simulator, for protection of the simulator, as shown in Figure 1.

Nebulizer and Face Mask

Examples of 3 types of nebulizers were chosen for testing: a constant-output nebulizer (Neb-Easy, Galemed, I-Lan, Taiwan), a breath-enhanced nebulizer (LC Plus, Pari Respiratory Equipment, Midlothian, Virginia), and a BAN (AeroEclipse, Trudell Medical, London, Ontario, Canada). Three pediatric aerosol masks were chosen: standard pediatric aerosol mask (Standard, Galemed, I-Lan, Taiwan), "Bubbles the Fish" aerosol mask (Fish, Pari Respiratory Equipment, Midlothian, Virginia), and a valved aerosol mask (Trudell Medical, London, Ontario, Canada).

Study Design

All 3 nebulizers were tested with both the standard and fish masks. However, since both masks are open to the atmosphere, the BAN was unable to be breath-actuated. Consequently, the AeroEclipse was manually actuated by depressing the manual button in synchrony with initiation of inspiration through to the end of inspiration, and with constant output by depressing the actuation button continuously throughout the breathing cycle. In addition, the BAN was breath-actuated when using the valved mask.

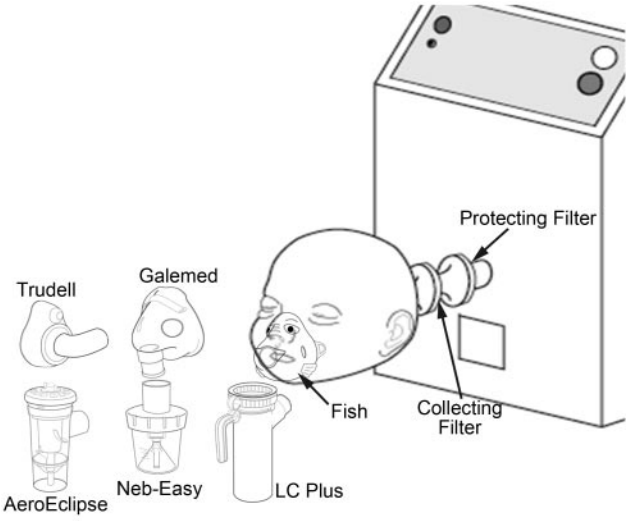

Fig. 1. Apparatus of experiment set up. The head and upper airway of the manikin were modified to allow placement of the inspiratory filter distal to the trachea.

Salbutamol sulfate (5.0 mg/2.5 mL, GlaxoSmithKline, Victoria, Australia) was diluted with distilled water for a total fill volume of 4 mL. Each nebulizer was powered by 50 psig oxygen gas at 8 L/min. Each condition was repeated ($n = 5$). Nebulizers were stopped when aerosol was not produced consistently (onset of sputter) for 5 seconds. The nebulization time was recorded for each run.

Aerosol Particle Size Distribution Measurement

Mass median aerodynamic diameter and geometric standard deviation were determined for each of the nebulizers in continuous output mode ($n = 3$), using an Andersen cascade impactor (ACI, Thermo Fisher Scientific, Waltham, Massachusetts) at an air flow of 28.3 L/min. The cascade impactor was disassembled after each test, and the drug was eluted with distilled water from the induction port (15 mL) and each stage and final filter (10 mL). The mass median aerodynamic diameter and geometric standard deviation were calculated in accordance with the United States Pharmacopoeia method.

Aerosol Measurement

Nebulizers were weighed using an electronic semi-micro balance (Sartorius, Göttingen, Germany) when dry, after filling with salbutamol, and then following nebulization. The nebulizers and inspiratory filters were washed/eluted with 5 mL of distilled water, while the aerosol masks and the mannequin face were washed with 10 mL of distilled water.

Samples were analyzed via spectrophotometry (Hitachi High-Technologies, Tokyo, Japan) at a wavelength of 276 nm. The spectrophotometer was set to zero by running solvent alone prior to each analysis. A simple linear regression and prediction were developed from doubling dilutions of a known salbutamol sulfate solution ($r^2 = 0.99$). The concentration of the sample solution and the amount of salbutamol were calculated from the concentration/absorbency relationship.

Statistical Analysis

Data were calculated by commercial statistical software (SPSS 17.0, SPSS, Chicago, Illinois). The normality of data distribution was analyzed, with the Kolmogorov-Smirnov test. The mean ± SD was calculated for each component of the drug mass eluted from the inspiration filter, the manikin face, the masks, and the nebulizer residual drug, as well as estimated ambient loss and nebulization time. The analysis of variance test was used and $P < .05$ was used for statistical significance. A Pearson correlation was performed to analyze the relationship of the drug mass on the face/mask and nebulizer.

Results

Table 1 shows the percent of total dose (mean ±SD) inhaled, retained in the nebulizer (dead volume), retained on the mask, and deposited on the face of the model, as well as the nebulization time of the 3 types of nebulizers with 2 masks. The fish mask produced significantly higher face deposition ($P = .001$), and mask deposition ($P < .001$) with all nebulizers tested. Manually breath-actuated nebulization resulted in the lowest inhaled dose and higher nebulization time ($P = .001$). With constant output the BAN delivered a greater inhaled dose than LC Plus ($P = .025$).

Table 2 shows percent of dose deposited (mean ± SD) for the BAN tested with 3 masks. Compared to breath-actuated nebulization, constant nebulization delivered 10–20-fold more drug to the inspiratory filter ($P < .001$). The retained drug in the nebulizer (dead volume) with constant nebulization was significantly less ($P < .001$). In comparison of masks under the breath-actuated nebulization model, aerosol delivery via a valved mask deposited a significantly higher dose on the mask.

Figure 2 illustrates the inhaled dose from the BAN with manual and breath actuation and continuous nebulization using the standard, fish, and valved masks. In all cases, constant-output deposition was greater than manual and breath-actuation ($P < .001$), and constant-output deposition was greater with the fish than the standard or valved mask, without significance ($P = .12$).

The mean ± SD of nebulization time was greater with the BAN, at 39 ± 5 min with breath-actuated nebulization, than 11 ± 3 min with constant nebulization ($P < .001$).

Table 1. Inhaled Dose, Dose Remaining in Nebulizer as Dead Volume, and Nebulization Time for 3 Nebulizers With the 2 Open to Atmosphere Masks

	Inhaled Dose, %		Retained Drug, %		Face Deposition, %		Mask Deposition, %		Time (min)	
	Standard	Fish	Standard	Fish	Standard	Fish*	Standard	Fish	Standard	Fish
Neb-Easy	6.7 ± 2.8	10.0 ± 3.1	57.1 ± 5.3	49. ± 4.8	1.1 ± 0.4	0.9 ± 0.2	1.5 ± 0.6	3.8 ± 0.8	9.9 ± 1.1	23.0 ± 0.8
LC Plus	5.7 ± 2.0	5.7 ± 2.5	57.2 ± 3.4	61.9 ± 5.2	1.2 ± 0.6	0.4 ± 0.2	0.9 ± 0.3	1.2 ± 0.4	9.0. ± 0.9	9.2 ± 1.4
AeroEclipse manual	0.4 ± 0.4†	0.5 ± 0.5†	58.4 ± 1.6	53.8 ± 7.2	1.1 ± 0.2	1.1 ± 0.3	0.7 ± 0.3	2.1 ± 0.5	23 ± 1.5†	23.6 ± 1.5†
AeroEclipse continuous	8.9 ± 1.2‡	10.8 ± 2.3‡	55.4 ± 3.8	54.4 ± 3.4	1.3 ± 0.2	0.8 ± 0.2	1.1 ± 0.5	2.3 ± 0.4	8.5 ± 1.0	8.5 ± 1.0

* $P = .001$ for Fish versus standard mask on face/mask deposition.
† $P = .001$ for all comparisons of nebulization.
‡ $P = .025$ for LC Plus versus breath-actuated nebulizer nebulizing throughout the breathing cycle on inhaled dose.

Table 2. Mean ± SD of Dose Deposition and Nebulization Time Among Different Nebulization and Masks

		Deposition, %	
	Mask	Breath-Actuated	Constant*
Inhaled†	Standard	0.4 ± 0.4	8.7 ± 1.2
	Fish	0.5 ± 0.5	10.8 ± 2.3
	Valved	1.0 ± 0.6	9.3 ± 0.4
Face	Standard	1.1 ± 0.2	1.3 ± 1.7
	Fish	1.1 ± 0.3	0.8 ± 0.2
	Valved	4.8 ± 1.4	9.1 ± 1.5
Mask	Standard	0.7 ± 0.3	1.1 ± 0.5
	Fish	2.0 ± 0.5	2.3 ± 0.3
	Valved‡	6.0 ± 2.0	4.4 ± 0.9
Dead volume†	Standard	58.4 ± 1.6	55.4 ± 3.8
	Fish	53.8 ± 7.2	54.4 ± 3.4
	Valved§	60.1 ± 2.5	42.1 ± 5.3
Ambient loss	Standard	49.5 ± 2.1	33.5 ± 3.5
	Fish	42.6 ± 0.8	37.8 ± 4.6
	Valved	28.1 ± 5.6	35.2 ± 10.5
Nebulization time, min†	Standard	23.0 ± 1.5	8.4 ± 1.0
	Fish	23.6 ± 3.3	8.5 ± 1.0
	Valved‖	39.9 ± 5.2	11.0 ± 3.3

Values are mean ± SD.
* $P < .001$ for breath actuated versus constant nebulization.
† $P < .001$ for breath-actuated versus constant nebulization for nebulization time, inhaled dose, and dead volume.
‡ $P < .001$ for valved mask versus standard and fish mask.
§ $P = .01$ for valved mask versus standard mask.
‖ $P < .001$ for valved mask versus standard and fish mask.

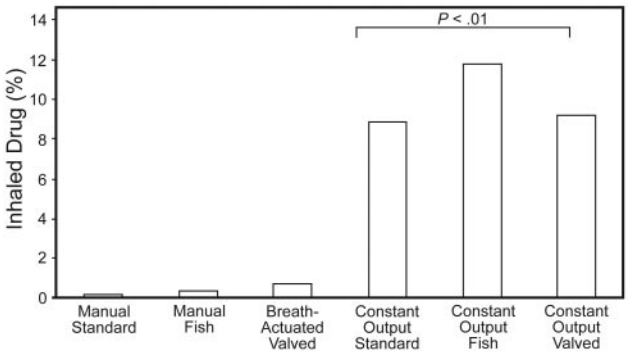

Fig. 2. Comparison of inhaled dose from the BAN with manual actuation, breath actuation, and continuous nebulization with the standard, fish, and valved masks.

Pearson correlation showed that drug deposited on the face and mask or on the inspiratory filter was in a negative relationship with the residual dose of the nebulizer, −0.2 and 0.96, respectively. The correlation of drug deposition between face, mask, and inspiration filter was 0.75. In other words, the more drug emitted by the nebulizer, the more drug deposited on the face, mask, and filter.

The mass median aerodynamic diameters ± geometric standard deviations were similar: Neb-Easy 2.47 ± 2.23 μm, Pari 2.87 ± 2.0 μm), AeroEclipse in continuous mode 2.93 ± 2.07 μm.

Discussion

To our knowledge, this is the first study to demonstrate that the use of breath-synchronized nebulization, whether manual or breath-actuated, provides substantially less aerosol delivered to the level of the trachea than continuous nebulization in a simulated 2–4-year-old, regardless of the type of mask used. In addition, the conventional constant-output jet nebulizer delivered similar to greater inhaled dose than the breath-enhanced nebulizer. The reported level of in vitro deposition with continuous nebulization in this study was similar to the in vivo lung doses, ranging from 4.8 to 8.2%, reported by Erzinger et al in 18–36 month old children breathing radio-tagged aerosol with properly fitting masks and relaxed tidal breathing.[7]

These findings are in contrast to results reported using adult and larger pediatric breathing parameters, in which breath actuation has consistently been associated with similar or greater inhaled dose than breath-enhanced or conventional jet nebulizers. Breath-actuated aerosol delivery to small infants and toddlers has long been suspect, due to

the combination of small tidal volumes, variable inspiratory flow patterns, short inspiratory times, and greater proportional anatomical dead space than adults.

When an infant or small child is unable to breath-actuate the BAN, clinicians may either manually actuate the nebulizer in synchrony with the child's inspiration or hold down the manual actuation to nebulize continuously. While it seems intuitive to expect that manual breath actuation would be more efficient than marginal breath actuating or continuous nebulization, these results clearly demonstrate the superiority of continuous nebulization in this population, by 10–20-fold.

While guidance by the BAN manufacturer suggests manual actuation of the nebulizer when a child cannot reliably breath-actuate the nebulizer, the instructions fall silent on how to determine whether the "appropriate" breath actuation is adequate to deliver an effective dose. It should be noted that in this study the model was able to consistently breath-actuate the BAN, and it was difficult to determine by casual observation specific variables that might impact the dose delivered. With a sinusoidal breathing pattern, in our study, the 20 L/min peak inspiratory flow exceeded the 15 L/min actuation threshold for the BAN; however, the requisite flow above threshold may occur late in the inspiratory cycle. This is further complicated by delays of aerosol generation from the time of actuation to full output of the aerosol generator, which may be as much as 60 ms with jet nebulizers.

Unlike previous models that collected inhaled dose at the face, this model collected aerosol distal to the anatomic structures of the naso/oro- and hypopharynx residing between the face and the trachea. Aerosol entering the airway must pass through the anatomic structures of the upper airway en route to the collecting filter distal to the trachea, resulting in impactive losses of aerosol at points of non-laminar or transitional flow, reducing dose available to the lung. In addition, the internal volumes of these anatomic structures approximate a substantial component of the anatomical dead space, so that aerosol that enters the airway during the last one third of inspiration is less likely to reach the filter at the trachea prior to end inspiration, and is subsequently exhaled. Both factors may contribute to the decreased deposition with manual actuation as well as breath actuation.

Using adult parameters, Rau et al reported inhaled doses of 14% with continuous output nebulizer, 13% with LC Plus, and 34% with the AeroEclipse.[5] In contrast, our results with small child parameters were $< 1\%$ of drug dose deposited beyond the upper airway with breath-actuated nebulization, while deposition with continuous nebulization with both the simple jet and the LC Plus nebulizer, delivery ranged from 5.7% to 10.8%.

Sangwan et al using scintigraphy to quantify inhaled and lung deposition in 3 adults, and reported that the MistyNeb continuous jet nebulizer had an inhaled dose of 19.4% and deposited 7.9% in the lung, while the BAN delivered 20.8% and 14.16%, respectively.[6] It should be noted that the BAN was operated with only 2 mL fill volume, versus 4 mL with the MistyNeb, yielding a lower ratio of the inhaled dose reported by Rau. As expected, the lung dose was substantially lower than the inhaled dose measured at the face, with the difference largely attributed to losses in the upper airway.

Barry and O'Challaghan compared breath-enhanced nebulizers, the LC Plus and the LC Star, in combination with different compressors. The amount of salbutamol collected on the filter delivered by the LC Plus was 19.8% with pediatric parameters.[12] However, we found approximately 5.7% in our study. This may be in part due to the point of aerosol sampling; while earlier studies measured inhaled mass at entry point of the model airway, we collected aerosol distal to the trachea of an anatomically correct model. As the upper airway is known to filter out inhaled aerosols, a lower level of tracheal deposition might be expected. Therefore, the inhaled drug dose was much less than other studies have reported.[5,9,10]

Manual actuation from beginning of inspiration to end of inspiration was based on simulator waveform. A short delay at beginning of the inspiration, due to hand-eye coordination, might have contributed to the difference and caused the insufficiency of the nebulizer. The lung stimulator was set with inspiratory time of 0.8 second; however, with a short delay of actuation, the aerosols might be generated with only as little as 0.6 seconds to reach the inspiratory filter before a breath was ended. A similar phenomenon occurred when the nebulizer was actuated with the valved mask. With a sinusoidal inspiratory flow waveform, the flow reached the highest point (20 L/min) in the middle of a breath. Consequently the inspiratory flow reached 15 L/min of critical flow rate for the valved mask at 0.2–0.3 second, so that aerosol generations began after the first one third of the breath had been delivered, with the last 0.1–0.2 seconds of aerosol generation filling anatomical dead space and being cleared with exhalation, reducing opportunities for deposition distal to the trachea. This may have been associated with the low inhaled dose ($< 1\%$) with both manual actuation and breath actuation under toddler parameters.

Bosco and colleagues compared the inhaled dose of the AeroEclipse and a breath-enhanced nebulizer (LC Star) by simulating tidal breathing patterns and parameters from 10 adult subjects, and compared deposition of drug at a filter placed between the nebulizer and the patient. They found similar drug amounts deposited on the filters with the AeroEclipse and LC Star (29.6% and 26.7%, respectively, in vitro, and 29.9% and 28.9%, respectively, in vivo).[10] The findings suggest a small but significant

underestimation of inhaled dose in vitro with the breath-enhanced nebulizer.

The nebulization time with the AeroEclipse during breath actuation was 2–3-fold longer than with the constant-output and breath-enhanced nebulizers. With breath actuation the AeroEclipse generates aerosol when flow of ≥ 15 L/min is reached or exceeded, which would increase treatment time.

Rau et al reported that, with adult breath parameters, ambient loss of aerosol was less with the AeroEclipse (6.6%), compared to the continuous output nebulizer (17–27%) and LC Plus (18.3%).[5] However, we found AeroEclipse with breath-actuated nebulization produced 39% ambient loss with the aerosol masks, and 28% with the valved mask. The valved mask resulted in 4-fold higher face deposition than the standard or fish mask during breath-actuated nebulization. The valved mask appears to contain aerosol between inspiration and expiration, which increased aerosol deposition both on the face and the mask.

A breath-enhanced nebulizer contains 2 one-way valves to minimize aerosol waste during the expiration phase. A patient entrains air through the nebulization chamber with the Pari LC inspiratory vent. Studies with adults and larger children have shown increased inhaled mass, by as much as 50%, over the continuous output nebulizers, and reduced aerosol waste to atmosphere.[5,9,11] Yet our results illustrate that the breath-enhanced nebulizer neither improved inhaled dose nor reduced the ambient loss with toddler breathing patterns. Possibly the inspiratory flow and time may not be sufficient to activate the one-way valves. Interestingly, the fish mask designed for use with the LC Plus provided the lowest facial deposition. A study suggested that the curved angle of the fish mask might be the element to reduce face deposition.[3] By contrast, drug deposited on the inspiratory filter with the fish mask was greater than with the standard mask with both the Neb-Easy and AeroEclipse during continual nebulization, but not with the LC Plus. Although breath actuation and manual breath synchronized actuation with the AeroEclipse produced the lowest inhaled dose (< 0.7%), continuous nebulization delivered a higher inhaled dose (8.3% vs 11.3%) than the Neb-Easy (5.2% vs 9.2%) or LC Plus (5.6% vs 5.8%) with the standard and fish mask, respectively.

Limitations

There are several limitations to this study. First, the parameters set on the breath simulator were designed to characterize a 2–4-year-old child; therefore, the results may not apply to other age ranges of children during aerosol therapy. In perusing the literature, it was difficult to find "normal" breathing patterns differentiated between toddlers and preschool children. We combined complementary characteristics previously described in the aerosol literature, in an attempt to bracket representative breathing parameters of the 2–4-year-old child.[14,15] Second, the consistent breathing patterns produced by the simulator was not intended to represent the highly erratic breathing patterns found with this patient population when awake or under stress.[13] In fact, we have used a breathing pattern that might be found during sleep, in which flows and frequency have been shown to be much more consistent.[13] The model used does not account for changes in breathing patterns or failure to tolerate a closely fitting mask, and may well overestimate aerosol drug delivery in vivo. This study was based on one set of breathing patterns, and does not provide specific guidance on the wide range of breathing parameters that may be encountered in clinical situations. Consequently, further in vitro study may be warranted to determine the parameter limits at which breath actuation will reliably result in improved inhaled doses in infants and young children, compared to continuous nebulization.

Clinical Implications

While many aerosol devices are primarily designed for use with adults and larger children, there is little guidance for their use with infants and toddlers. Our findings suggest that simply being able to breath-actuate the BAN with a simulated small child does not assure effective aerosol delivery. Similarly, manually actuating the BAN in synchrony with inspiration did not improve the inhaled dose. The choice to provide breath actuation or continuous nebulization can make a 20-fold difference in the dose reaching the lungs. As casual observation by the operator of "breath actuation" yielded such low deposition fractions for the breathing pattern tested, these findings suggest that clinical criteria for using continuous versus breath-actuated nebulization require further evaluation.

Further studies will be required to provide clinicians guidance as to when breath actuation may be more effective than continuous nebulization in infants and small children.

Conclusions

In summary, with this model simulating a 2–4-year-old child's breathing pattern, the AeroEclipse, when used as a breath-actuated or manually actuated breath-synchronized nebulizer, delivered only a small fraction of the inhaled tracheal dose achieved with continuous aerosol generation by all of the nebulizers tested. The combination of low inhaled dose and long treatment times suggest that breath-actuated nebulization is not as effective as continuous aerosol generation in these younger children who appear to be able to consistently breath-actuate the nebulizer. Aerosol

mask design can impact inhaled drug dose across the range of nebulizers tested. Further in vitro trials should be done to explore the range of breathing patterns in which breath actuation is less effective than continuous aerosol generation.

REFERENCES

1. Amirav I. Infant aerosol holding chamber face masks: not all are born equal! Respir Care 2006;1(2):123-125.
2. Amirav I, Mansour Y, Mandelberg A, Bar-Ilan I, Newhouse MT. Redesigned face mask improves "real life" aerosol delivery for Nebuchamber. Pediatr Pulmonol 2004;37(2):172-177.
3. Lin HL, Restrepo RD, Gardenhire DS, Rau JL. Effect of face mask design on inhaled mass of nebulized albuterol, using a pediatric breathing model. Respir Care 2007;52(8):1021-1026.
4. Iles R, Lister P, Edmunds AT. Crying significantly reduces absorption of aerosolised drug in infants. Arch Dis Child 1999;81(2):163-165.
5. Rau JL, Ari A, Restrepo RD. Performance comparison of nebulizer designs: constant-output, breath-enhanced, and dosimetric. Respir Care 2004;49(2):174-179.
6. Sangwan S, Condos R, Smaldone GC. Lung deposition and respirable mass during wet nebulization. J Aerosol Med 2003;16(4):379-386.
7. Erzinger S, Schueepp KG, Brooks-Wildhaber J, Devadason SG, Wildhaber JH. Facemasks and aerosol delivery in vivo. J Aerosol Med 2007;20(Suppl 1):S78-S83, discussion S83-S84.
8. Esposito-Festen JE, Ates B, van Vliet FJ, Verbraak AF, de Jongste JC, Tiddens HA. Effect of a facemask leak on aerosol delivery from a pMDI-spacer system. J Aerosol Med 2004;17(1):1-6.
9. Lin YZ, Huang FY. Comparison of breath-actuated and conventional constant-flow jet nebulizers in treating acute asthmatic children. Acta Paediatr Taiwan 2004;45(2):73-76.
10. Bosco AP, Rhem RG, Dolovich MB. In vitro estimations of in vivo jet nebulizer efficiency using actual and simulated tidal breathing patterns. J Aerosol Med 2005;18(4):427-438.
11. Leung K, Louca E, Coates AL. Comparison of breath-enhanced to breath-actuated nebulizers for rate, consistency, and efficiency. Chest 2004;126(5):1619-1627.
12. Barry PW, O'Callaghan C. An in vitro analysis of the output of salbutamol from different nebulizers. Eur Respir J 1999;13(5):1164-1169.
13. Janssens HM, van der Wiel EC, Verbraak AF, de Jongste JC, Merkus PJ, Tiddens HA. Aerosol therapy and the fighting toddler: is administration during sleep an alternative? J Aerosol Med 2003;16(4):395-400.
14. Dolovich MB. Assessing nebulizer performance. Respir Care 2002;47(11):1290-1301, discussion 1301-1304.
15. Jauernig J, Mitchell J, Berg E, Dennis J, Kreher C, Lamb P, et al. Position paper: recommendation on the adoption of breathing patterns for infants and small children in general chapter 2.9.44. Preparations for nebulization. Pharmeur Sci Notes 2008;(1):31-32.