Effect of Face Mask Design on Inhaled Mass of Nebulized Albuterol, Using a Pediatric Breathing Model

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BACKGROUND: Aerosol face mask design and the distance at which the face mask is held from the face affect the delivery of nebulized medication to pediatric patients. OBJECTIVE: To measure the inhaled mass of nebulized albuterol with 3 types of pediatric face mask, at 3 different distances from the face, with a model of a spontaneously breathing infant. METHODS: We compared a standard pediatric face mask and 2 proprietary pediatric face masks (one shaped to resemble a dragon face, the other shaped to resemble a fish face). The albuterol was nebulized with a widely used jet nebulizer. Aerosol delivery with each type of mask was measured with the mask at 0 cm (ie, mask directly applied to the mannequin face), 1 cm, and 2 cm from the mannequin face. In each test the nebulizer was filled with a 3-mL unit dose of albuterol sulfate and powered by oxygen at 8 L/min, with a total nebulization time of 5 min. The mannequin face was connected to a lung simulator that simulated a spontaneously breathing infant. We measured inhaled mass by collecting the aerosol on a 2-way anesthesia filter that was attached to the back of the mannequin's oral opening via a 15-mm silicon adapter. We also measured residual drug left in the nebulizer, and estimated the drug lost to the atmosphere. RESULTS: The mean ± SD inhaled percentage of the nominal dose values at 0 cm, 1 cm, and 2 cm, respectively, were 2.18 ± 0.53%, 1.45 ± 0.46%, and 0.92 ± 0.51% with the standard mask; 2.65 ± 0.55%, 1.7 ± 0.38%, and 1.3 ± 0.37% with the dragon mask; and 3.67 ± 0.8%, 2.92 ± 0.4%, and 2.26 ± 0.56% with the fish mask. With all 3 masks there was a statistically significant difference ($p < 0.001$) in inhaled mass between the 0 cm and 2 cm distance. The fish mask had a significantly higher ($p < 0.001$) inhaled mass than the dragon mask or the standard mask, at all 3 distances. CONCLUSIONS: The inhaled mass of albuterol is significantly reduced when the mask is moved away from the face. The fish mask had significantly higher inhaled mass than the standard mask or the dragon mask, under the conditions we studied. Mask design may affect nebulized albuterol delivery to pediatric patients. *Key words: albuterol, aerosol, face mask, inhaled drug mass, pediatric, jet nebulizer.* [Respir Care 2007;52(8):1021–1026. © 2007 Daedalus Enterprises]

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Introduction

Gas-powered jet nebulizers are commonly employed to deliver medications to patients' airways via a mouthpiece or a face mask. Although no significant difference in clinical response has been found in adults between a mouthpiece and a fitted mask,[1] administering nebulized medication with a fitted face mask to infants and toddlers can be quite challenging. As infants grow older, they are increasingly aware of their surroundings and frequently become distressed with the application of a mask. When the child is upset, the seal between the face and the mask is easily broken, which causes entrainment of ambient air and decreases the quantity and the concentration of aerosol inhaled.[2,3]

An alternative technique for aerosol delivery to the pediatric patient is "blow-by," in which the clinician aims the aerosol flow toward the patient's face instead of applying a mask. We previously reported a 43% reduction in the inhaled dose with a 1-cm gap between the mask and the inhalation hole on a mannequin face, and a 67% reduction with 2-cm gap.[4] Similar data were previously found by Everard et al.[5]

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There are several pediatric face masks available for use with jet nebulizers. Research on the efficiency of face masks with a metered-dose inhaler (MDI) with spacer/holding chamber suggests that the choice of face mask and the integrity of the interface between the mask and the child's face is critical in determining the inhaled dose in children.[6–11] Newly redesigned masks for MDIs allow a better seal with the patient's face. The pediatric face masks used with jet nebulizers have traditionally been smaller versions of the masks used with adults. These pediatric masks have a considerably larger volume of potential dead space and relatively large side holes, compared to adult face masks. Manufacturers have designed pediatric face masks in an effort to improve drug delivery to children. In our preliminary literature search, we found a paucity of reports on inhaled drug mass with jet nebulizers attached to pediatric face masks of various designs.

The purpose of the present study was to determine the inhaled drug mass, nebulizer residual drug loss, and estimated ambient loss during delivery of nebulized albuterol to 3 brands of pediatric face mask, with the mask at 0 cm, 1 cm, and 2 cm from a mannequin face connected to a breathing simulator, with the breathing pattern of a spontaneously breathing infant.

Fig. 1. Configuration of equipment for simulation of pediatric breathing and nebulized albuterol delivered via face mask, with the mask at 0 cm, 1 cm, and 2 cm from the chin of the mannequin face.

Methods

Lung Model

A model of a spontaneously breathing infant was created with a lung simulator (ASL [Active Servo Lung] 5000, IngMar Medical, Pittsburgh, Pennsylvania). The simulator was set at a maximum muscle pressure of 13.5 cm H_2O, a resistance of 20 cm H_2O/L/s, and a compliance of 5 mL/cm H_2O, to generate a tidal volume of 60 mL. The respiratory rate was set at 20 breaths/min, inspiratory time was 0.7 s, inspiratory-expiratory ratio was 1:3, and inspiratory flow was 120 mL/s.

A mannequin face with a 15-mm silicon adapter was attached to the inhalation filter (a 2-way, nonconductive anesthesia filter, model 1T0241, Baxter Healthcare, Deerfield, Illinois), which collected the inhaled aerosol. A similar filter was attached to the lung simulator, for protection from inhaled aerosol, but was not used to calculate drug loss. Figure 1 shows the setup.

Study Design

A nebulizer (Misty-Neb, Baxter Healthcare Corporation, Valencia, California) was attached to a standard face mask (Hudson RCI, Durham, North Carolina), then to a mask designed to resemble a dragon face (DragonMask, KidsMED, Hinsdale, Indiana), and then to a mask designed to resemble a fish face (Bubbles the Fish, PARI Respiratory Equipment, Monterey, California) (Table 1).

Each nebulizer was held in a vertical orientation with a metal holder and a clamp to prevent error from misalignment. All masks were held perpendicular to the inhalation filter inlet.

Each trial was conducted by placing the face mask at 0 cm (ie, the mask was in contact with the mannequin face), 1 cm, or 2 cm from the mannequin face, measured

Table 1. Features of 3 Pediatric Aerosol Masks

	Standard Pediatric Aerosol Face Mask	Dragon Aerosol Face Mask	Fish Aerosol Face Mask*
Picture			
Manufacturer	Hudson	KidsMED	Pari Respiratory Equipment
Length (cm)	9.52	9.52	10.16
Width (cm)	6.35	6.98	7.62
Mask volume (mL)†	85	70	75
Diameter of side holes (cm)‡	2	1	1

*Designed specifically for use with PARI nebulizers.
†Mask volume was measured by filling the mask with water.
‡Holes on both sides.

from the lower edge of the mask to the chin of the mannequin face. Aerosol delivery with each type of mask was measured at the 3 distances.

To minimize variations among masks and among distances caused by nebulizers, we used 5 different Misty-Neb nebulizers. Each nebulizer was used with all 3 mask types and at all 3 distances, so each nebulizer was run a total of 9 times, in random order; thus, there were 45 separate trials.

All the nebulizers were powered by 50 psi oxygen at 8 L/min. Gas flow to the nebulizer was started immediately after the first simulator breath. Then, 100 simulated breaths were run, in 5 min; then the gas flow was terminated in synchrony with the simulator. In each trial the nebulizer was filled with a 3.0-mL unit dose of albuterol sulfate, which contains 2.5 mg of albuterol base.

Measurements

The inhaled drug mass was measured by extracting the aerosol from the inhalation filter. In bench models, the inhalation filter is placed in the final path of aerosol that would be inhaled by a patient.[12] Each nebulizer was weighed before and after filling with albuterol, and following nebulization, to determine the amount of solution remaining in the device (dead volume). The dead volume was collected by washing the nebulizer system components with 0.1 normal hydrochloric acid solution (JT Baker, Phillipsburg, New Jersey). The dead volume was then analyzed via spectrophotometry (Beckman Instruments, Fullerton, California), using a known amount of solvent added to the dead volume. To avoid contamination with residual albuterol, after each trial the mask and the mannequin face were wiped with an alcohol pad, and the 15-mm silicon adapter was washed and dried.

Because of the open nature of the model (ie, because of the open space between the mask and the mannequin face), some aerosol was lost to the ambient air, so that aerosol could not be collected and measured. Instead, it was calculated by subtracting the inhaled drug mass and the dead volume drug mass from the starting (nominal) dose of albuterol sulfate.

A simple linear regression and prediction equation were developed from a known albuterol sulfate solution (Sigma, St Louis, Missouri). All drug amounts were analyzed via spectrophotometry (Beckman Instruments, Fullerton, California), at a wavelength of 276 nm. The solvent was 0.1 normal hydrochloric acid solution. The inhalation filter was washed for 1 min, with gentle agitation. The spectrophotometer was calibrated prior to trials, with a holmium oxide filter (Beckman Instruments, Fullerton, California) to determine the wavelength accuracy, and set to zero by running the solvent alone before each analysis. The concentration of the sample solution and the amount of albuterol were calculated from a known concentration/absorbency relationship.

Statistical Analysis

Means and standard deviations were calculated (SPSS 11.5, SPSS, Chicago, Illinois) for each component of the total drug mass, nebulizer loss, and estimated ambient loss. A 2-way factorial analysis of variance (ANOVA) was performed for the masks and distances, with an alpha

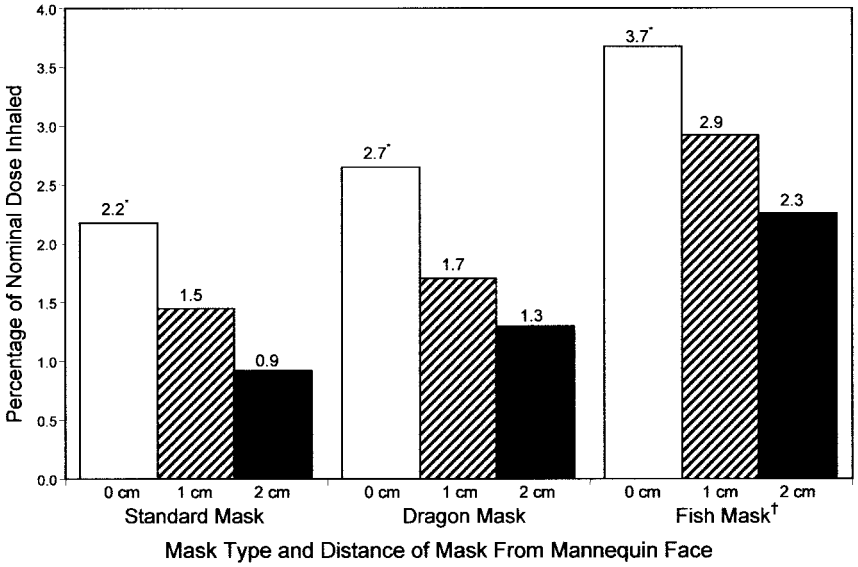

Fig. 2. Mean inhaled percentage of nominal dose with 3 types of face mask and 3 distances from the mannequin face. The differences between the fish mask and both the standard mask and the dragon mask were significant at all distances. Inhaled percentage of nominal dose was significantly greater with all masks at 0 cm than at 2 cm. * $p < 0.001$ for all comparisons of 0 cm versus 2 cm. † $p < 0.001$ for fish mask versus standard mask and dragon mask at all distances.

level of 0.05.[13] Follow-up comparisons of each device at each distance were performed using 1-way ANOVA with Bonferroni adjustment.

We calculated the effect size, which is an index of the magnitude of a treatment effect. Unlike tests for significance, measures of effect size in ANOVA determine the degree of association between variables and the effect of the dependent variable. We used the partial eta squared (η^2) value to estimate the degree of association between the samples.

Results

Table 2 lists the mean ± SD values for the percent of the nominal dose collected on the inhalation filter, left in the nebulizer, and lost to the ambient air, for each type of mask, at 0 cm, 1 cm, and 2 cm.

A 1-way factorial ANOVA with Bonferroni adjustment for masks and distances indicated a statistically greater inhaled drug mass with the fish mask than with the standard mask or the dragon mask, overall ($p < 0.001$), and significant decrease in inhaled drug mass as distance increased ($p < 0.001$).

Figure 2 shows the percentage of the nominal dose values collected on the inhalation filter. Bonferroni comparisons of the 3 masks showed significant differences ($p < 0.001$) in inhaled drug mass between the standard mask and the fish mask, and between the fish mask and the dragon mask. However, there was no significant differ-

Table 2. Drug Mass on the Inhalation Filter, Left in the Nebulizer, and Estimated Ambient Loss

	Distance (cm)	Mean ± SD Percent of Nominal Dose		
		Standard Mask	Dragon Mask	Fish Mask*
Inhalation filter	0†	2.18 ± 0.53	2.65 ± 0.55	3.67 ± 0.80
	1†	1.45 ± 0.46	1.70 ± 0.38	2.92 ± 0.40
	2†	0.92 ± 0.51	1.30 ± 0.37	2.26 ± 0.56
Nebulizer residual drug	0	66.22 ± 4.59	66.97 ± 1.76	65.51 ± 2.74
	1	70.30 ± 3.80	66.00 ± 7.29	68.90 ± 6.73
	2	66.38 ± 4.86	67.22 ± 6.16	67.72 ± 5.14
Estimated ambient loss	0	31.60 ± 4.05	30.38 ± 4.08	30.82 ± 2.50
	1	28.25 ± 3.82	32.30 ± 7.13	28.18 ± 6.74
	2	32.70 ± 4.55	31.48 ± 2.31	30.02 ± 5.50

*Significant difference overall ($p < 0.001$).
†Significant difference overall across distances ($p < 0.001$).

ence between the standard mask and the dragon mask. The partial η^2 was 0.617 compared among the 3 distances, and 0.591 compared among the 3 masks, which indicates that the probability of nonoverlap among the 3 groups is approximately 33–38%, according to Cohen's standard.[14]

Discussion

The results of this in vitro study indicate that the inhaled drug mass with the fish mask was significantly higher than with the standard mask or dragon mask. Furthermore, our results are consistent with previous studies that reported a significant drop in the inhaled drug mass when the mask was moved away from the face.[4–11,15,16]

The standard pediatric aerosol mask is a smaller version of the adult mask and has a considerably larger dead space than the fish mask or dragon mask. The 2-cm side holes in the standard mask allow more aerosol particles to escape during nebulization. The side-holes on the dragon mask are 1 cm in diameter, so, theoretically, less aerosol should be lost than with the standard mask, but our results do not support that theory. The lower inhaled drug mass with the standard mask and dragon mask may be due to aerosol inertia (the tendency of an object to travel in a straight line once it is moving). In the standard mask and the dragon mask, the aerosol enters the mask traveling upwards, towards the top of the mask, and inertia may cause the aerosol particles to impact the inner surface of the mask, whereas with the fish mask the aerosol travels directly toward the nasal/oral area (Fig. 3). In a previous study that compared inhaled drug mass delivered via T-piece versus via standard pediatric mask, we found a higher inhaled drug mass with the T-piece.[4] The T-piece is constructed with a 90° angle, with a nebulizer that directs the aerosol stream toward the patient's face. Because of this physical design, we hypothesized that the inhaled drug mass with the T-piece, with or without distancing the mask from the mannequin face, was greater than with all of the masks we used in the present study.

Sangwan and collaborators[15] nebulized radiolabeled normal saline to an infant breathing model. They used 7 commercially available face masks interfaced with 3 compatible fitting nebulizers, to compare the facial deposition of aerosol. The fish mask in combination with the Pari LC Plus nebulizer had the highest inhaled drug mass, at 6.0% of the nominal dose. It also had one of the lowest eye and facial aerosol depositions. The combination of the Hudson mask and the Misty-Neb nebulizer resulted in 66% less inhaled drug than the combination of the fish mask and the Pari LC Plus nebulizer.[15] In a similar study, Smaldone and colleagues nebulized 0.25 mg of budesonide to a pediatric breathing model. They found that the combination of the fish mask and the Pari LC Plus yielded about 65% higher inhaled drug mass than the combination of the standard mask and the Hudson Updraft II jet nebulizer.[16]

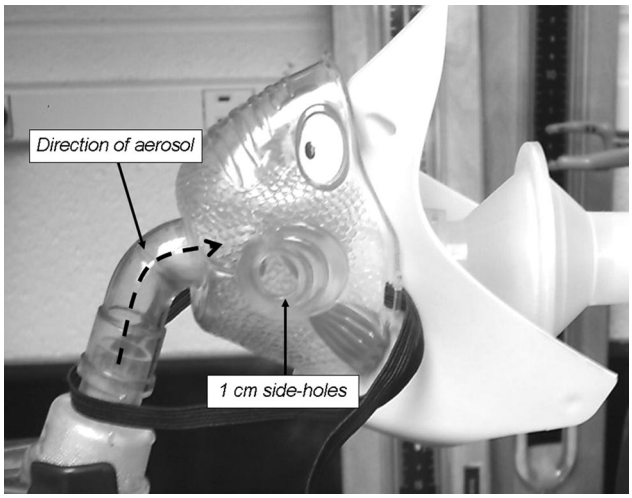

Fig. 3. Aerosol trajectory with the fish mask. With the fish mask the aerosol is aimed more directly at the nasal/oral area than with the standard mask or the dragon mask.

The standard mask and dragon mask direct the aerosol to the upper portion of the mask, whereas the fish mask directs the aerosol towards the nasal/oral area (see Fig. 3). We hypothesize that the difference in angle of aerosol entry into the mask influences inhaled mass, because aiming the aerosol more directly at the nasal/oral area reduces aerosol impact on the mask. A recent 3-dimensional numerical study by Shakked et al[17] on the administration of aerosolized drugs to infants via a hood supports our theory of the importance of directing the aerosol toward the nasal/oral area. Shakked et al found that the number of aerosol particles that penetrated the nostrils of their infant model significantly decreased the further away the aerosol funnel was from the nostrils.[17]

It is also possible that a better face seal is created with the fish mask, by the extended cover on the face. Also, the fish mask's smaller side holes may keep more aerosol particles in the mask during the treatment time and reduce loss to the ambient air.

Though several studies have reported data on inhaled drug mass when the face mask is moved away from the face model,[4–11,15,16] we found only 3 studies that evaluated the impact of leak between the pediatric mask and the face on inhaled drug mass when the aerosol is generated via jet nebulizer.[4,5,16] Our previous study reported data that compared the inhaled drug mass with a standard mask versus with a T-piece at 0 cm, 1 cm, and 2 cm from the inhalation filter.[4] However, in that study, albuterol nebulization was run to the onset of sputtering, with no tapping of the nebulizer. The mean inhaled percentage of the nominal dose with the standard aerosol mask at 0 cm (2.88%), 1 cm (1.61%), and 2 cm (1.3%) in that study[4] compares well to the present results with the standard mask: 2.18%, 1.45%, and 0.92%, respectively. The present study values also compare well to those

found by Everard et al, who nebulized 4 mL (40 mg) of sodium cromoglycate. Their mean percentage of the nominal dose values at 0 cm, 1 cm, and 2 cm were 3.13%, 1.2%, and 0.45%, respectively.[5] Smaldone et al[16] quantified in vitro the influence of the face mask on the inhaled mass of budesonide from jet nebulizers and pressurized MDIs with valved holding chambers. The configuration that lacked mask/face seal was associated with significantly lower inhaled mass than the sealed mask/face configuration, with both the MDIs and the nebulizers.[16]

A recent report by Shah et al, which evaluated force-dependent static dead space of face masks used with valved holding chambers, reinforced the importance of both the mask design and the integrity of the mask/face seal.[8] The mask's ability to seal to the face was evaluated by applying different forces. Although the masks that allowed more force to obtain a better seal were more flexible and associated with a greater reduction of the mask dead space volume, Shah et al cautioned about the possible impact of the mask pressure on the child's face, because the mask pressure could offset the benefit of the improved aerosol delivery obtained by a better mask/face seal.

There are several limitations to the present study. Erratic breathing because of crying is frequent in infants and toddlers receiving aerosol.[3] The steady-state nature of an in vitro study does not reflect the potential differences one might expect when studying human subjects. A second limitation was the lack of a true mass/balance measurement, because we were unable to capture aerosol lost to the ambient air. It is theoretically possible that some aerosol collected on the filter could be lost during exhalation back through the filter, which would lead to underestimation of the inhaled drug mass. However, we believe such loss is negligible, because liquid aerosol particles are collected on the filter. Another limitation was our use of a preset nebulization time, instead of nebulizing until sputter. According to a study by Rau et al, the expected average nebulization time with the Misty-Neb with 3 mL at 8 L/min is approximately 12 min.[18] We used a preset nebulization time of 5 min to provide a consistent aerosol output, for better comparison. Hence, the percentage of inhaled drug mass on the inhalation filter in the present study may underestimate the real percentage patients actually get, because our nebulization time is probably shorter than actual nebulization time in the clinic, and nebulization might therefore be considered incomplete. And, finally, we did not measure aerosol particle size. Although particle size measurements can be obtained separately, such measurements may not be representative of particle sizes in in vitro testing or actual lung deposition in a human subject.

Conclusions

Our data suggest that holding the aerosol mask away from the child's face (the "blow-by" technique) should be reevaluated as a clinical strategy for delivering aerosolized medication to children. Also, the design of the face mask affects nebulized aerosol delivery to pediatric patients. Clinical research is necessary to determine whether the design of nebulizers or face masks affects clinical response. These findings may be useful for interpreting future clinical studies on face mask delivery of aerosolized drugs to pediatric patients.

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REFERENCES

1. Hess D. Nebulizers: principles and performance. Respir Care 2000; 45(6):609–622.
2. Collies GG, Cole CH, LeSouef PN. Dilution of nebulised aerosols by air entrainment in children. Lancet 1990;336(8711):341–343.
3. Iles R, Lister P, Edmunds AT. Crying significantly reduces absorption of aerosolised drug in infants. Arch Dis Child 1999;81(2):163–165.
4. Restrepo RD, Dickson SK, Rau JL, Gardenhire DS. An investigation of nebulized bronchodilator delivery using a pediatric lung model of spontaneous breathing. Respir Care 2006;51(1):56–61.
5. Everard ML, Clark AR, Milner AD. Drug delivery from jet nebulizers. Arch Dis Child 1992;67(5):586–591.
6. Hayden JT, Smith N, Woolf DA, Barry PW, O'Callaghan C. A randomised crossover trial of facemask efficacy. Arch Dis Child 2004;89(1):72–73.
7. Amirav I, Mansour Y, Mandelberg A, Bar-Ilan I, Newhouse MT. Redesigned facemask improves "real life" aerosol delivery for Nebuchamber. Pediatr Pulmonol 2004;37(2):172–177.
8. Shah SA, Berlinski AB, Rubin BK. Force-dependent static dead space of face masks used with holding chambers. Respir Care 2006; 51(2):140–144.
9. Amirav I, Newhouse MT. Aerosol therapy with valved holding chambers in young children: importance of the face mask seal. Pediatrics 2001;108(2):389–394.
10. 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.
11. 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.
12. Smaldone GC. Drug delivery via aerosol systems: concept of "aerosol inhaled." J Aerosol Med 1991;4(3):229–235.
13. Kirk RE. Experimental design: procedures for the behavioral sciences. Belmont CA: Brooks/Cole Publishing Co; 1994:237–244.
14. Cortina JM, Nouri H. Effect size for ANOVA designs. Iowa City: Sage Publications; 2000:1.
15. Sangwan S, Gurses BK, Smaldone GC. Facemasks and facial deposition of aerosols. Pediatr Pulmonol 2004;37(5):447–452.
16. Smaldone GC, Berg E, Nikander K. Variation in pediatric aerosol delivery: importance of facemask. J Aerosol Med 2005;18(3):354–363.
17. Shakked T, Broday DM, Katoshevski D, Amirav I. Administration of aerosolized drugs to infants by a hood: a three-dimensional numerical study. J Aerosol Med 2006;19(4):533–542.
18. Rau JL, Ari A, Restrepo RD. Performance comparison of nebulizer designs: constant-output, breath-enhanced, and dosimetric. Respir Care 2004;49(2):174–179.