In-vitro Comparison of 4 Large-Volume Nebulizers in 8 Hours of Continuous Nebulization

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BACKGROUND: Continuous albuterol nebulization has become the standard of care for patients with status asthmaticus. Predictable albuterol delivery is paramount for effective therapy. We compared the aerosol characteristics, solution output, and albuterol output of 4 brands of large-volume nebulizer. METHODS: We studied 6 units of the following nebulizer brands: AirLife Misty Finity (Cardinal Health), Flo-Mist (Smith's Medical), Heart (WestMed), and Hope (B&B Medical Technologies). All the nebulizers were operated according to the manufacturers' recommendations and connected to 180-cm of flexible corrugated tubing. We diluted 80 mg of albuterol sulfate nebulizer solution in saline solution, per the manufacturer's recommendations (admixture required to deliver 10 mg/h). Solution output, solution retained in the tubing, reservoir albuterol concentration, and albuterol output were determined hourly for 8 hours. The ambient and aerosol temperatures were recorded every 30 minutes. The target outputs were ± 20% of the manufacturer's specification. Aerosol characteristics were determined via cascade impaction, with aerosol collected between 60 and 70 min of operation. RESULTS: All the aerosols had an adequate size for pulmonary deposition. The increase in reservoir albuterol concentration was < 20% for the first 4 hours. There were no significant differences in achieving the target albuterol output, but none of the nebulizers achieved the target albuterol output during the 1st hour. Albuterol output was similar between the nebulizers for the first 5 hours. There were no differences in reaching the target solution output. The Misty Finity and Hope had a solution output consistent with the manufacturers' specifications. The amount of solution retained in the tubing was greatest with the Heart (23%); other nebulizers' tubing-retained-solution ranged from 6–9%. Albuterol output corrected for the tubing-retained solution rendered similar results. Aerosol temperature decreased with aerosol production and increased in the corrugated tubing, but was below the ambient temperature at the patient interface. CONCLUSIONS: The tested nebulizers had similar performance during the first 5 hours. The nebulizer solution might need to be replaced if treatment is planned for longer period. The Misty Finity and Hope nebulizers had a more consistent solution output. *Key words: nebulizer; nebulization; aerosol; particle size; albuterol.* [Respir Care 2010;55(12):1671–1679. © 2010 Daedalus Enterprises]

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Introduction

Asthma is a chronic disease that affects a substantial part of the population. Twenty-two million people are diagnosed with asthma in the United States. About half of them will experience an exacerbation each year. Asthma affects an estimated 6 million children. Moreover, 4000 asthma-related deaths occur every year in the United States.[1] The management of severe asthma exacerbation includes steroids, bronchodilators, and oxygen. Patients who do not respond to frequent albuterol and ipratropium bromide inhalation are considered in status asthmaticus and are given albuterol via continuous nebulization. Currently, continuous albuterol nebulization is the standard of care for patients in status asthmaticus in the intensive care unit.[2] Previous research demonstrated its efficacy, safety, and time-saving characteristics.[3-5] Status asthmaticus is one the most common indications for admission to pediatric intensive care units.[6]

In vivo and in vitro studies showed that albuterol can be delivered via small-volume nebulizer connected to a continuous drip or via large-volume nebulizer.[7-11] We previously showed that the aerosol characteristics of large-volume nebulizers remain constant for the first 4 hours.[9] A large-volume nebulizer allows continuous nebulization of albuterol for up to 8 hours without reloading the bronchodilator solution. The duration of continuous albuterol nebulization depends on the patient's clinical response and can range from a few hours to a few days. Current practice includes periodic assessment of the patient's clinical status and the nebulizer's solution by the respiratory therapist. If therapy is needed for more than 8 hours, the nebulizer is emptied and a fresh bronchodilator solution is loaded. At our institution the nebulizer is changed after 48 hours of use. Several characteristics are important to review when deciding which nebulizer to use. The aerosol particle size needs to be appropriate for pulmonary deposition; solution output and albuterol output should remain constant; and the reservoir albuterol concentration should be low. Accuracy of delivery and reliable performance are crucial to be able to interpret the patient's clinical response. A previous study documented substantial performance differences among small-volume nebulizers.[12] No data are available in that regard for large-volume nebulizers. We compared the aerosol characteristics, albuterol output, and solution output of 4 brands of commercially available large-volume nebulizer. We hypothesized that the different brands would exhibit different performances.

Methods

Nebulizers

We studied 6 units from the same lot of the following nebulizer brands: AirLife Misty Finity (Misty) (Cardinal Health, McGaw Park, Illinois), Flo-Mist (Smiths Medical, Dublin, Ohio), Heart (WestMed, Tucson, Arizona), and Hope (B&B Medical Technologies, Loomis, California) (Fig. 1). All these nebulizers are single-patient-use devices. At the time of this study, these brands were the only large-volume (200–240 mL loading volume) nebulizers marketed in the United States for 8 hours of continuous delivery of bronchodilator. After the laboratory phase of this study, we conducted a cost comparison and found that Misty, Flo-Mist, and Hope had comparable pricing, but Heart was more expensive. All the nebulizers were operated with central oxygen directly, vertically connected to a calibrated flow meter (Timeter by Allied, Allied Healthcare Products, St Louis, Missouri). Flow-meter output was verified with a mass flow meter (4043, TSI, Shoreview, Minnesota) set to measure oxygen. The nebulizers were connected to flexible standard corrugated tubing (180 cm long, 22 mm inner diameter) and operated at the flows recommended by the manufacturers (Table 1).

Fig. 1. Large-volume nebulizers studied. From left to right: Flo-Mist, Heart, Misty Finity, Hope.

Table 1. Operating Flows and Loading Volumes

Brand	Operating Flow (L/min)	Loading Volume for 8 h Operation (mL)
Airlife Misty Finity	11	240
Flo-Mist	13	200
Heart	10	240
Hope	10	200

Nebulizer Solution

We diluted 16 mL of 0.5% albuterol sulfate nebulizer solution (80 mg) (Hi-Tech Pharmacal, Amityville, New York) in either 224 mL (for the Misty and Heart nebulizers, albuterol concentration 0.33 mg/mL) or 184 mL (for the Flo-Mist and Hope nebulizers, albuterol concentration

0.4 mg/mL) of normal saline solution. These nebulizers loaded with the above-referenced solutions and operated per the manufacturers' recommendations deliver 10 mg albuterol per hour, according to the nebulizers' package inserts.

Particle Size Distribution

To determine aerosol particle size we used an impactor (Next Generation, MSP, Shoreview, Minnesota) at a flow of 15 L/min (Fig. 2).[13] We used a mass flow meter (4043, TSI, Shoreview, MN) connected to the impactor's throat to calibrate the impactor before refrigeration. Before each impactor run we cooled the impactor to 4°C for 90 min to minimize the possible effects of changes in ambient humidity and evaporation due to heat loss during impactor operation.[14,15] The flow was verified and the impactor run was started within 5 min of removal from the refrigerator. The nebulizer was connected via corrugated tubing to the impactor, and the impactor was operated for 10 min, during minutes 60–70 of nebulizer operation, to allow enough albuterol to be collected. The connection between the tubing and the impactor throat was loose to allow air entrainment, because the nebulizer operating flow was lower than the impactor flow. The impactor temperature remained below the aerosol temperature during the testing interval (Fig. 3). The albuterol captured in the impactor was diluted with ultrapure water and analyzed via spectrophotometry (Biomate 3, Thermo Electron, Waltham, Massachusetts) at 276 nm.[9]

We calculated mass median aerodynamic diameter (MMAD), geometric standard deviation (GSD), and percentage of particles smaller than 5 μm, according to the United States Pharmacopeia and European Pharmacopeia recommendations, with cascade impactor software (CITDAS V3, Copley Scientific, Nottingham, United Kingdom).[16,17] The particle-size experiments were done in quadruplicate.

Solution Output and Albuterol Output

We weighed (CS2000 scale, Ohaus, Pine Brook, New Jersey) the nebulizer before loading the solution ($Weight_{dry}$) and after loading the solution ($Weight_0$). We then extracted a 1-mL aliquot from the nebulizer reservoir to measure the starting albuterol concentration. Then once an hour for 8 hours we re-weighed the nebulizer and extracted another 1-mL aliquot to measure the albuterol concentration at that point.

We measured the albuterol concentration in the extracted aliquots via spectrophotometry. We normalized the data by the initial concentration and express it as percentage of the initial concentration, to avoid the confounding factor of slightly different initial concentrations.

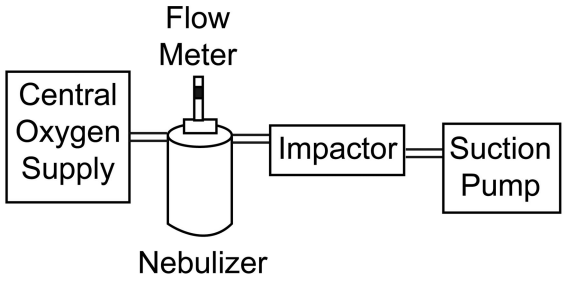

Fig. 2. Experimental setup to measure aerosol particle size.

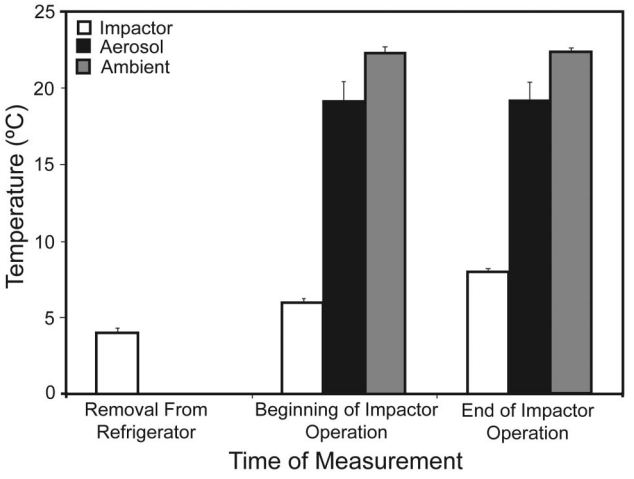

Fig. 3. Impactor and aerosol temperature.

We calculated the albuterol output as the difference between the product of the concentration and the solution at 2 different time points. For instance, the albuterol output in the 1st hour is:

$$[(Weight_0 - Weight_{dry}) \times Concentration_0] - [(Weight_1 - Weight_0 - 1\ g) \times Concentration_1]) \quad (1)$$

where $Weight_0$ is the nebulizer weight after adding the albuterol solution but before extracting the first aliquot or operating the nebulizer, $Weight_{dry}$ is the nebulizer dry weight before adding any albuterol solution, $Weight_1$ is the nebulizer weight after 1 hour of operating the nebulizer, 1 is the mass of the 1 mL extracted for measurement of albuterol, $Concentration_0$ is the albuterol concentration of the first aliquot (extracted before operating the nebulizer), and $Concentration_1$ is the albuterol concentration of the 2nd aliquot (extracted at the end of 1 hour of nebulizer operation). The target albuterol output was ± 20% of the manufacturers' specified albuterol output, which was 10 ± 2 mg/h for all 4 brands.

The solution output was determined with a gravimetric method. The loading volume was calculated as:

$$\text{Weight}_0 - \text{Weight}_{dry} \quad (2)$$

The solution output in the 1st hour was calculated[18] as:

$$\text{Weight}_1 - (\text{Weight}_0 - 1\ \text{g}) \quad (3)$$

The target solution output was ± 20% of the manufacturer's specified solution output, which was 25 mL/h for the Flo-Mist and Hope nebulizers, and 30 mL/h for the Misty and Heart nebulizers. These data were also normalized as percentage of target output.

Aerosol Temperature

We conducted another set of experiments with 3 units of each nebulizer brand. We slightly modified the setup to incorporate simultaneous measurement of the aerosol temperature immediately adjacent to the nebulizer ($T_{proximal}$) and at the patient interface (T_{distal}) (Fig. 4). We loaded the Misty and Heart nebulizers with 240 mL of normal saline solution, and the Flo-Mist and Hope nebulizers with 200 mL of normal saline solution. We weighed each nebulizer and the corrugated tubing separately, and then connected the nebulizer to the calibrated flow meter and operated it with oxygen at the manufacturer's recommended flow (see Table 1). We re-weighed the nebulizer and corrugated tubing every hour for 8 hours. We measured $T_{proximal}$ and T_{distal} every 30 min with a dual-probe thermometer (Duotemp 400, Fisher & Paykel, Auckland, New Zealand). We measured the ambient temperature ($T_{ambient}$) with another calibrated thermometer (Humidity Temperature Meter, General Tools & Instruments, New York, New York). We re-tested the Heart nebulizer with an elbow connecting the nebulizer to the corrugated tubing in an abbreviated protocol (4 hours).

Tubing Retention

We calculated the amount of solution that was retained in the tubing (the tubing retention [in percent]) as:

$$[(\text{Final circuit weight} - \text{initial circuit weight})/(\text{initial nebulizer weight} - \text{final nebulizer weight})] \times 100\% \quad (4)$$

Albuterol Output at the Patient Interface

We calculated the amount of albuterol delivered to the patient (the albuterol output at the patient interface) as:

$$\text{Albuterol output} \times [(100 - \text{tubing retention})/100] \quad (5)$$

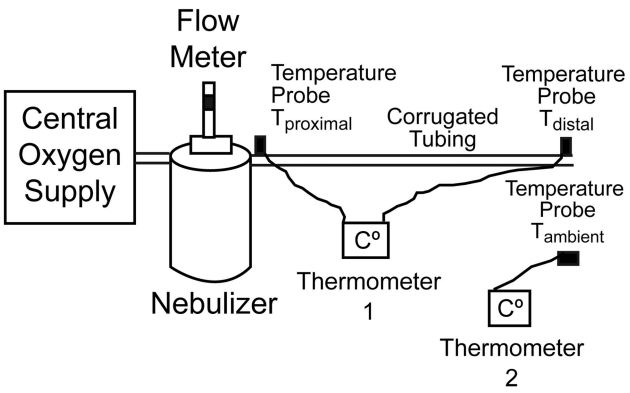

Fig. 4. Experimental setup to measure aerosol temperature and tubing retention.

Statistical Analysis

We compared the hourly solution output, tubing retention, albuterol output, albuterol output at patient interface, and reservoir albuterol concentration within brands with analysis of variance (ANOVA) for repeated measures, and conducted post-hoc analysis with Tukey's test when necessary. We compared categorical data (solution output and albuterol output) with the chi-square test. We compared particle size, solution output, tubing retention, albuterol output, albuterol output at the patient interface, and reservoir albuterol concentration between brands with ANOVA, and conducted post-hoc analysis with Tukey's test when necessary. A $P < .05$ was considered statistically significant. The analysis was done with statistics software (MDAS 2.0, EsKay Software, Silver Spring, Maryland).

Results

Particle Size Distribution

The mean ± SD MMADs of the Hope and Heart nebulizers were similar (3.31 ± 0.03 μm and 3.35 ± 0.15 μm, respectively) and larger than that of the Flo-Mist and Misty nebulizers (2.48 ± 0.12 μm and 2.57 ± 0.09 μm, respectively) ($P < .001$ via ANOVA, followed by Tukey's test with $P < .05$) (Table 2). The GSD range was 2.22–2.24 μm ($P = .99$ via ANOVA). The percentage of particles smaller than 5 μm was similar for the Heart and Hope nebulizers (64.3 ± 2.7% and 68.1 ± 1%, respectively) and smaller than that of the Misty and Flo-Mist nebulizers (79.7 ± 2.6% and 77.5 ± 1.6%, respectively) ($P < .001$ via ANOVA, followed by Tukey's test with $P < .05$).

Reservoir Albuterol Concentration

All the nebulizers showed a progressive increase in reservoir albuterol concentration over 8 hours. The increase was > 20% after the 5th hour for all nebulizers. The

Table 2. Aerosol Particle Size

Brand	MMAD (μm)*	GSD*	% < 5 μm*†
Airlife Misty Finity	2.57 ± 0.09‡	2.24 ± 0.09	79.7 ± 2.6§
Flo-Mist	2.48 ± 0.12‡	2.22 ± 0.09	77.5 ± 1.6§
Heart	3.35 ± 0.15	2.22 ± 0.38	64.3 ± 2.7
Hope	3.31 ± 0.03	2.24 ± 0.15	68.1 ± 1.0

* Mean ± SD of 4 measurements.
† Percentage of particles smaller than 5 μm.
‡ Smaller than Heart or Hope ($P < .001$ via analysis of variance).
§ Larger than Heart or Hope ($P < .001$ via analysis of variance).
MMAD = mass median aerodynamic diameter
GSD = geometrical standard deviation

Flo-Mist developed a substantially higher reservoir albuterol concentration than the other nebulizers between the 4th and 7th hours (Fig. 5).

Solution Output

The mean ± SD solution outputs of the Misty and Hope were within 20% of the manufacturers' reference values (28.4 ± 4.2 mL and 22 ± 1.6 mL, respectively). Conversely, the Heart and Flo-Mist solution outputs were more than 20% outside the manufacturers' reference values (27.4 ± 8.9 mL and 27.2 ± 3.1 mL, respectively) (Fig. 6). However, when compared as a categorical event (ie, within 20% of the target solution output), there were no significant differences. When each nebulizer was analyzed for hourly output, the Hope showed no difference ($P = .02$ via repeated-measures ANOVA, but the difference became nonsignificant after multiple comparison analysis). The Flo-Mist showed a decreased output in the 8th hour versus the 1st through 6th hours, and in the 7th versus 6th hour ($P < .001$ via repeated-measures ANOVA), the Misty showed a decreased output in the 8th versus the 1st through 7th hours ($P < .001$ via repeated-measures ANOVA), and the Heart showed a decreased output in the 8th versus the 4th hour ($P = 0.3$ via repeated-measures ANOVA (see Fig. 6).

Tubing Retention

Tubing retention did not significantly change during nebulization ($P = .015$ via ANOVA, but not significant after Tukey's test: $P = .11$, $P = .7$, and $P = .91$ for Misty, Flo-Mist, Heart, and Hope, respectively). Tubing retention differed among the devices: Misty had the lowest tubing retention (5.9 ± 1.6%, Tukey's test $P < .05$ versus the others), Heart had the highest (23.3 ± 4.7%, Tukey's test $P < .05$ versus the others), and Hope and Flo-Mist were intermediate (9.2 ± 2.3% and 9.3 ± 4.1%, respectively, Tukey's test $P > .05$ between them). In the additional test with the elbow connector between the nebulizer and the tubing, the tubing retention with the Heart decreased to 15.6 ± 8.6% ($P = .03$).

Albuterol Output

When albuterol output was considered as a categorical event (ie, albuterol output within 20% of the target), there were no significant differences. None of the nebulizers achieved the target albuterol output during the 1st hour. There were no significant differences in hourly albuterol output among the nebulizers between the 1st and 5th hours, or in the 7th hour. In the 6th hour the Flo-Mist's albuterol output was significantly higher than that of the Heart or Hope ($P = .004$ via ANOVA, followed by Tukey's test, $P < .05$). In the 8th hour the Hope's albuterol output was significantly higher than that of the Flo-Mist ($P = .004$ via ANOVA, followed by Tukey's test, $P < .01$) (Fig. 7).

Albuterol Output at the Patient Interface

Between the 4 nebulizer brands there were no significant differences in hourly output at the patient interface in the 1st through 5th hours, or in the 7th hour. In the 6th hour the Flo-Mist's output at the patient interface was significantly higher than that of the Heart or Hope ($P < .001$ via ANOVA, followed by Tukey's test, $P < .05$). In the 8th hour the Hope's output at the patient interface was significantly higher than that of the Flo-Mist or Heart ($P = .002$ via ANOVA, followed by Tukey's test, $P < .05$) (Fig. 8).

Aerosol Temperature

T_{distal} remained unchanged with the Hope (19.9 ± 0.6°C, $P = .63$). All the other nebulizers had a significantly higher initial T_{distal}, compared to the temperatures between 30 min and the end of nebulizer operation (21.3 ± 1.5°C vs 19.1 ± 1.4°C for Misty, 21.4 ± 0.9°C vs 18.7 ± 1.0°C for Flo-Mist, and 20.4 ± 1.4°C vs 19.9 ± 0.6°C for Heart, $P < .001$ for all nebulizers).

The differences between $T_{proximal}$ and $T_{ambient}$ were −10.8 ± 1.1°C for Hope, −10.5 ± 0.5°C for Flo-Mist, −10.2 ± 0.7°C for Misty, and −9.1 ± 0.7°C for Heart.

The differences between $T_{ambient}$ and T_{distal} at 60 min of nebulization were 3.6 ± 1.2°C for Flo-Mist, 3.2 ± 1.7°C for Misty, 1.9 ± 0.3°C for Heart, and 3.7 ± 1.5°C for Hope.

Discussion

We compared the aerosol characteristics, solution output, and albuterol output of 4 large-volume nebulizers. All the nebulizers produced heterodisperse aerosols with particle size characteristics optimal for pulmonary deposition, and all had similar albuterol output during the first 5 hours. Misty and Hope had a more consistent solution output.

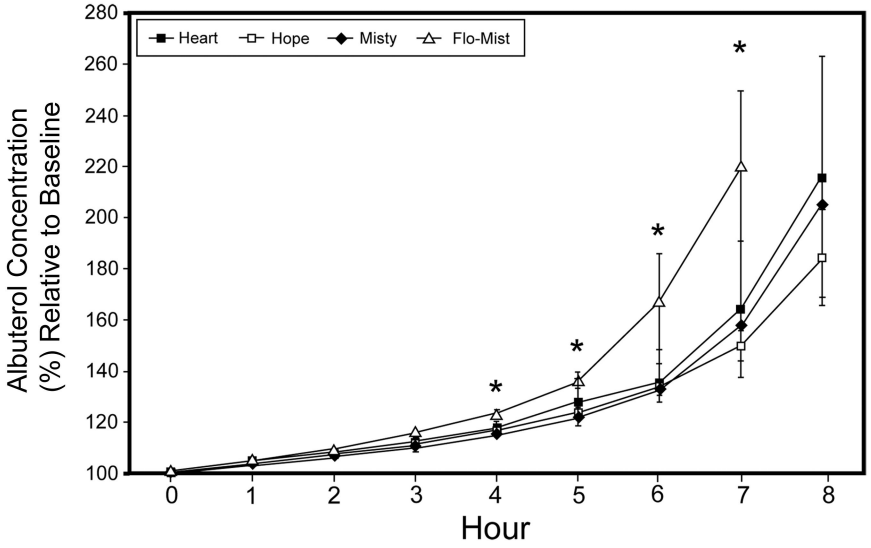

Fig. 5. Reservoir albuterol concentration. Data normalized to initial concentration. * Albuterol concentration was highest with the Flo-Mist. The data points represent the mean values, and the error bars represent the standard deviations.

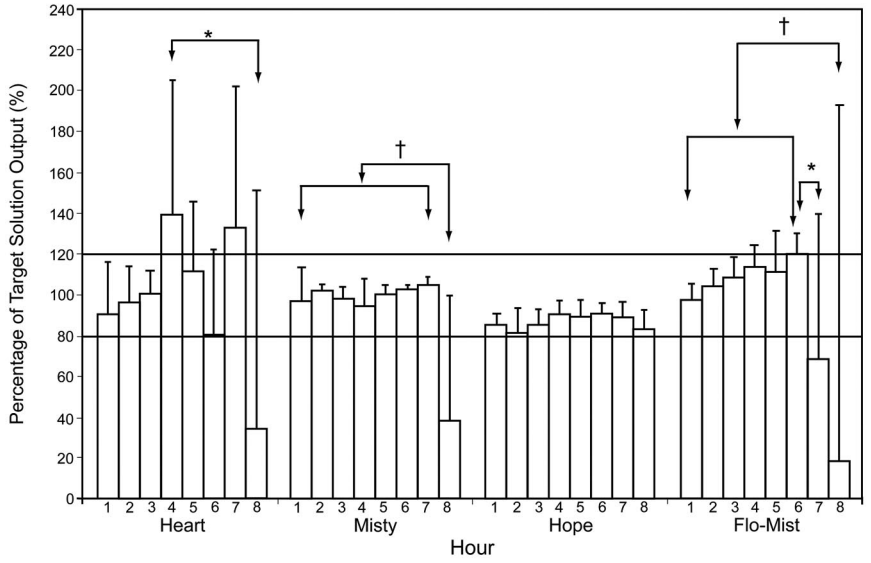

Fig. 6. Solution output. Data normalized to manufacturer's specifications. The horizontal lines at 80% and 120% represent the target solution output. With the Heart the solution output in the 8th hour was lower than that in the 4th hour. With the Misty the solution output in the 8th hour was lower than that in the 1st through 7th hours. With the Flo-Mist the solution output in the 8th hour was lower than that in the 1st through 6th hours, and the solution output in the 7th hour was lower than that in the 6th hour. * $P < .05$ via Tukey's test. † $P < .001$ via Tukey's test. The bars represent the mean values, and the error bars represent the standard deviations.

Reservoir albuterol concentration had increased significantly after 5 hours, and the different nebulizers had different tubing retentions.

Aerosol Characteristics

All the aerosols were suitable for pulmonary deposition.[19] This finding was expected because the approval process these devices undergo through the United States Food and Drug Administration requires proof that a new device has characteristics similar to a previously approved device.[20] Hope and Heart had larger MMADs (3.31 μm and 3.35 μm, respectively) than Flo-Mist and Misty (2.48 μm and 2.57 μm, respectively). The former had a particle size ideal for aerosolized bronchodilators, as previously determined by other investigators.[21-23]

McPeck et al studied the aerosol characteristics of the Heart nebulizer and 2 small-volume nebulizers.[10] They reported a smaller particle size (2.12 μm) and slightly smaller GSD (2.47 μm) for the Heart nebulizer. The par-

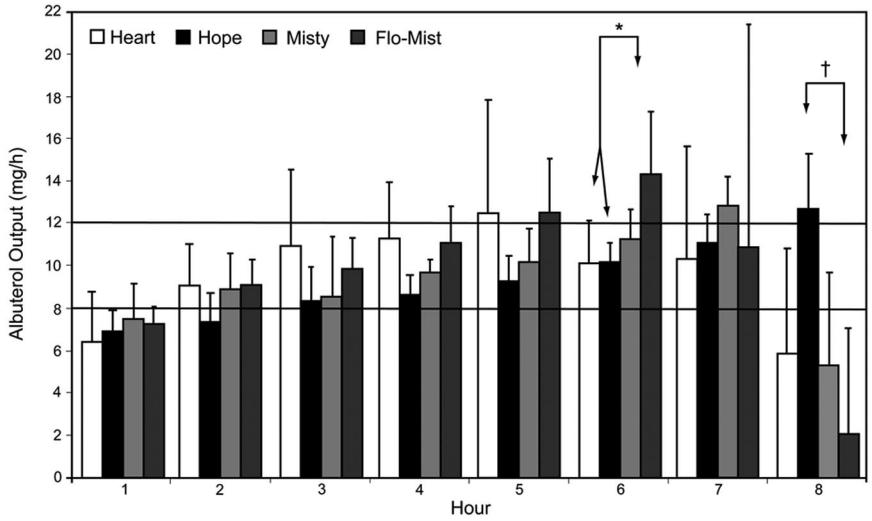

Fig. 7. Albuterol output. * Flo-Mist had a higher albuterol output than Heart or Hope in the 6th hour. † Hope had a higher albuterol output than Flo-Mist in the 8th hour. The bars represent the mean values, and error bars represent the standard deviations.

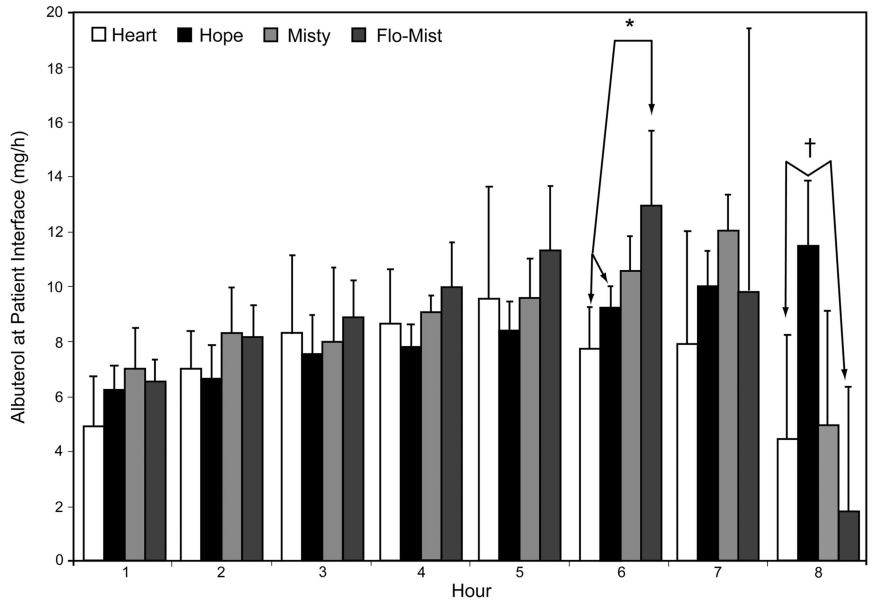

Fig. 8. Albuterol output at the patient interface. * Flo-Mist had a higher patient-interface albuterol output than Heart or Hope in the 6th hour. † Hope had a higher patient-interface albuterol output than Flo-Mist or Heart in the 8th hour. The bars represent the mean values, and the error bars represent the standard deviations.

ticle size differences between that study and ours could be because of different experimental setups. McPeck et al used a breathing simulator, and the aerosol was drawn from a T-piece that connected the nebulizer and the cascade impactor. In our study, as in clinical practice, the nebulizer was connected to the cascade impactor via a 180-cm corrugated tube. McPeck et al operated the impactor at room temperature, which may under-size the aerosol due to thermal transfer from the impactor to the aerosol. We used a cooled impactor technique to minimize that phenomenon.[14,15]

Raabe et al, in a characterization of the Heart nebulizer, reported an MMAD of 2 μm and a GSD of 2.6 μm.[11] The differences with our study could be explained by 3 reasons. First, Raabe and colleagues connected the nebulizer to the cascade impactor with tubing that was 30 cm long and with an inner diameter of 22 mm, whereas we used 180 cm of standard corrugated tubing. Second, Raabe et al used an unspecified brand of 7-stage cascade impactor operated at an undisclosed flow, whereas we used a Next Generation Impactor at 15 L/min. The latter has published archival data for its operation at 15 L/min, and it is con-

sidered more appropriate for the measurement of nebulized formulations. Third, Raabe et al operated their impactor at room temperature, whereas we used a cooled impactor, with the above-discussed consequences. In summary, the Hope and Heart had a better aerodynamic profile for albuterol delivery.

Reservoir Albuterol Concentration

The reservoir albuterol concentration determines the albuterol mass output, assuming a constant solution output and air entrainment. Therefore, a low reservoir albuterol concentration will help create a more constant albuterol output. In this study the reservoir albuterol concentration increased 15–24% after 4 hours, and 21–36% after 5 hours (see Fig. 5), which is similar to a previous study in which it increased 30% after 4 hours of continuous nebulization.[9] In the present study the Flo-Mist had the highest albuterol-concentration effect of the tested nebulizers. Raabe et al reported an albuterol-concentration increase of 200% with the Heart after 8 hours of continuous operation,[11] which is comparable to our finding of a 216 ± 47% concentration increase with the Heart. Although previous data were available for the Heart, the present study is the first to report on the Flo-Mist, Hope, and Misty. Concentration of the reservoir solution could have adverse effects, such as β-agonist stimulation, which could lead to arrhythmia, and the hypertonicity of the solution could lead to coughing or irritation,[24,25] though the latter does not seem very likely because albuterol provides bronchoprotection against inhaled hypertonic solutions; Delvaux et al prevented bronchoconstriction, provoked by inhalation of 4.5% hypertonic saline, by administering nebulized albuterol.[26]

Albuterol Output

Albuterol output was similar between the nebulizers for the first 5 hours. There were no significant differences in their achievement of hourly target albuterol output, but none of the nebulizers achieved the target albuterol output during the 1st hour. We cannot offer an explanation for this finding, but we speculate that it could be related to the large loading volume.

Solution Output

The Misty and Hope nebulizers showed a consistent solution output, as indicated by their small standard deviation values. The other nebulizers showed larger solution-output variability. Reisner et al studied the solution output of a different large-volume nebulizer and found it to be stable over a 4-hour operation.[27] However, they used saline instead of albuterol mixed with saline, as in our study and in patient care. We previously reported a constant output of albuterol solution over 4 hours with a modified Puritan Bennet jet nebulizer.[9] Raabe et al reported a solution output of 30 ± 1 mL/h with the Heart nebulizer operated at 10 L/min.[11] In the present study the Heart had a solution output of 27.4 ± 8.9 mL.

We speculate that the large standard deviation in solution output and albuterol output after 6 hours with some nebulizer brands might represent inter-nebulizer variability, as was previously reported for small-volume nebulizers.[28,29]

Tubing Retention

There were significant differences in tubing retention, but there was no correlation between operating flow and tubing retention. One potential explanation is that the tubing-retention differences are due to the different angles of the output connection port these nebulizers have. The best and worse performers in this category (Misty and Heart, respectively) have output-port angles of 90° and 180°, respectively (see Fig. 1). Flo-Mist and Hope had similar tubing retention and have similar output-port angle (45°). The differences in output-port angle could affect aerosol impaction against the tubing walls. Our 4-hour study of the Heart nebulizer with an elbow connector between the nebulizer and the tubing supports this hypothesis. Also, with the Misty, Flo-Mist, and Hope the nozzle is inside a cylindrical sleeve that communicates with the reservoir, whereas the Heart's nozzle is inside the reservoir, which might provide a less turbulent aerosol and filter larger particles, thereby decreasing the likelihood of aerosol impaction in the tubing. We assume that tubing retention significantly decreases albuterol delivery to the patient. Our findings underscore the need for manufacturers to provide aerosol characterization of their nebulizers and to specify the intended clinical setup. Raabe et al reported delivery efficiency to the mask of about 90% with the Heart nebulizer.[11] In the present study the efficiency was only 77%. We speculate that that difference is due to the difference in tubing length in the studies (30 cm vs 180 cm) and the difference in testing time (5 min vs 60 min and hourly for 8 h). Also, they applied continuous suction at 17 L/min, whereas we had no flow interacting with the nebulizer output.

Aerosol Temperature

The aerosol temperature decreased during aerosol-production and increased while traveling through the corrugated tubing, but was below ambient temperature at the patient interface. Other researchers have documented the temperature drop with small-volume nebulizers, but no data were available for large-volume nebulizers.[30] Phipps

et al reported that the temperature difference between aerosol and ambient was 11–15°C when operating the nebulizer at 8 L/min, and 5–6°C at low flow.[30] In our study the temperature difference range was 6.6–12.7°C with flows of 10–13 L/min. It appears that there is a plateau for this phenomenon at higher flows.

Limitations

We determined albuterol output as the difference in the albuterol mass remaining in the reservoir, instead of capturing the aerosol on a filter at the patient interface. However, we applied a correcting factor (tubing retention) to overcome that limitation. Another limitation is that the nebulizers were operated with continuous flow, without interaction of simulated breathing. Others have found a difference in albuterol output with different breathing patterns.[10]

Conclusions

The large-volume nebulizer brands we tested showed similar consistent albuterol output and solution output for the first 5 hours. Therefore, changing the nebulizer solution should be considered if the nebulizer will be operated beyond 5 hours. Misty and Hope had a more consistent solution output.

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