In Vitro Comparison of the Circulaire and AeroTee to a Traditional Nebulizer T-Piece with Corrugated Tubing

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BACKGROUND: Nebulizers are a popular means of delivering aerosolized medication, primarily albuterol, to the bronchial airways of patients, and there has been extensive research done on numerous nebulizers used with nebulizer T-pieces and corrugated tubing. Very little research has been performed on other types of nebulizer delivery systems and there is no substantial information on how effective various nebulizer delivery systems are in terms of the quantity and particle size of aerosolized medication delivered to the patient. In this study the Circulaire and the AeroTee, two devices that rely on bags to store aerosol during patient exhalation, are evaluated and compared to the conventional nebulizer T-piece with corrugated tubing. METHODS: Three each of the nebulizer T-piece with corrugated tubing, the Circulaire, and the AeroTee were sampled using 3 Vixone nebulizers. Each one of the 3 nebulizer delivery systems used the same 3 Vixone nebulizers. Each nebulizer delivery system was evaluated by connecting a constant-flow vacuum and compressed gas source cycled to simulate patient breathing at a respiratory rate of 14 breaths/min and an inspiration-expiration ratio of 1:2. Medication delivered was determined by sampling a portion of the simulated patient’s flow onto a membrane filter and calculating the total medication received by the patient. Particle size was determined by sampling with a cascade impactor under ambient conditions. RESULTS: The Circulaire delivered significantly less medication than the nebulizer T-piece with corrugated tubing (p < 0.001), whereas the AeroTee delivered substantially more medication than the nebulizer T-piece with corrugated tubing (p < 0.001). The particle size delivered by the Circulaire was significantly smaller than that of the nebulizer T-piece with corrugated tubing (p < 0.001), whereas the AeroTee delivered particle size equivalent to a nebulizer T-piece with corrugated tubing (p = 0.82). CONCLUSION: There are clinically important differences between nebulizer delivery systems. When evaluating the optimum means for delivering aerosolized medication, equal consideration should be given to both the brand of nebulizer and the nebulizer delivery system. [Respir Care 2000;45(3):313–319] Key words: nebulizer, aerosol, Circulaire, AeroTee, bronchodilator, aerodynamic particle size.
mizing the retention of carbon dioxide. The Circulaire uses a one-way flapper valve to prevent the backflow of any exhaled gas into the aerosol storage bag. The AeroTee uses a purging technique to effectively flush all retained carbon dioxide from the aerosol storage bag prior to inhalation. The present study compares the performance of these two new nebulizer delivery systems to the traditional nebulizer T-piece with corrugated tubing.

Methods

Nebulizer Delivery Systems Evaluated

Figure 1 shows the three nebulizer systems evaluated. Three of each nebulizer delivery system were selected, along with three Vixone nebulizers (Westmed, Tucson, Arizona). The Vixone nebulizer was selected for this study because, unlike the AeroTee, which may be used with any small volume nebulizer, the Circulaire comes equipped only with the Vixone and is not available without it. Both the Circulaire and the AeroTee use a 750 mL bag to store aerosol during exhalation so that the stored aerosol is delivered to the patient on the subsequent inhalation. The two devices differ in the manner in which they prevent the patient from rebreathing exhaled gas. The Circulaire (Fig. 2) uses a one-way flapper valve so that gas can travel only from the direction of the aerosol storage bag toward the patient, thus ensuring that exhaled gas goes directly from the patient to the ambient environment. The AeroTee (Fig. 3) allows some exhaled gas to enter the aerosol storage bag, which is then effectively purged by aerosolized medication using a coherent laminar jet prior to the beginning of inhalation. The nebulizer T-piece with corrugated tubing (Fig. 4) does not use collapsible aerosol storage means of any sort, but relies on the corrugated tubing (~ 60 mL) to capture some of the aerosol produced by the nebulizer during exhalation.
Evaluation of Quantity of Medication Delivered to the Patient and Total Treatment Time

Each of the three sets of nebulizer delivery systems were tested with the same three Vixone nebulizers. Each of the Vixone nebulizers was tested initially with a different nebulizer delivery system to prevent any bias in data due to deterioration in performance of the nebulizer after multiple uses. Prior to each test, each nebulizer was rinsed with filtered water, dried with compressed air, and filled with 3 mL of normal saline containing 2.5 mg of albuterol sulfate (Sigma, St Louis, Missouri) and 3.0 mg of fluorescein (Sigma, St Louis, Missouri). Despite the fact that Hess et al showed increasing medication delivery with increases in fluid volume, 3 mL of fluid was used for each test because that is what is still most commonly used under clinical conditions. As described by the manufacturer of the Vixone nebulizer, each nebulizer was set up and run at 6 L/min until all visual evidence of aerosol ceased and sputtering had ceased. Total treatment time was recorded. Simulated patient conditions were achieved with two solenoid valves, one attached to a compressor and one to a vacuum pump (Fig. 5). The solenoid valves were controlled by the function generator, which was set to cycle on a breathing rate of 14 breaths/min with a constant inspiration-expiration ratio (I:E) of 1:2. The flows of the compressed gas (exhalation) and the vacuum source (inhalation) were set to simulate a minute ventilation of 10 L/min (inhalation flow 30 L/min, exhalation flow 15 L/min). Prior to each test, a Wright Mark 14 respirometer (Ferraris, England) was used to verify that the volume of gas inhaled was equivalent to the volume of gas exhaled (tidal volume = 714 mL ± 5%). Each nebulizer and accompanying delivery device was attached via a mouthpiece to 22 mm tubing, the middle of which was equipped with a T-piece for sampling aerosol at 1.0 L/min through a 47 mm membrane filter (Micro Filtration Systems, Dublin, California). The opposite end of the 22 mm tube was equipped with a Y-piece, the branches of which led to the inhalation and exhalation solenoid valves. The dead space volume between the Y-piece and the mouthpiece of the nebulizer delivery system was measured to be approximately 50 mL.
The flow of simulated exhalation gas was shown to purge the dead space volume in approximately 0.2 second, so as to ensure that minimal aerosol was sampled during the exhalation phase. Sampling occurred continuously throughout the entire treatment time. Fluorescein collected was measured using a spectrophotometer (Barnstead, Dubuque, Iowa). Medication delivery rates were calculated from the product of the total amount of mass collected and the ratio of the inspiratory flow to the sampling flow.

**Evaluation of Aerodynamic Particle Size**

As with the evaluation of quantity of medication delivered, each of the three sets of nebulizer delivery systems was tested with the same three Vixone nebulizers. Each of the Vixone nebulizers was tested initially with a different nebulizer delivery system to prevent any bias in data due to deterioration in nebulizer performance after multiple uses. Prior to each test, each nebulizer was rinsed with filtered water, dried with compressed air, and then filled with 3 mL of normal saline containing 2.5 mg of albuterol sulfate and 3.0 mg of fluorescein. The nebulizer was run at 6 L/min. Aerosol was sampled at a flow of 0.7 L/min using a 7-stage cascade impactor (In-Tox Products, Albuquerque, New Mexico) immediately proximal to the mouthpiece as the aerosol exited into ambient room conditions. Aerodynamic cut-off sizes for the stages of the cascade impactor were 6.19 μm, 3.89 μm, 2.5 μm, 2.0 μm, 1.31 μm, 0.85 μm, and 0.40 μm, in addition to a membrane filter that captured all aerosol < 0.40 μm. The relative amount of medication collected on each stage of the cascade impactor was determined fluorometrically using the spectrophotometer. MMAD was then calculated from a best-fit plotting of cumulative mass percentage versus aerodynamic diameter on log-probability graph paper, using the spectrophotometer data for each cascade impactor stage.

**Percent of Aerosol Delivered in the 1–5 μm Range**

The percent of aerosol delivered in the 1–5 μm range was determined directly from the cascade impactor particle sizing data. Because the cascade impactor did not have stages with aerodynamic cutoffs at exactly 1 μm and 5 μm, results were logarithmically interpolated using the relative mass collected for the stages immediately around 1 μm and 5 μm, as is consistent with cascade impactor data.

**Mass of Aerosol Delivered in the 1–5 μm Range**

The mass of aerosol delivered in the 1–5 μm range was calculated as the percent of aerosol between 1 μm and 5 μm, multiplied by the medication rate determined previously, and represents the amount of medication most available for deposition to the bronchial airways and alveoli.1–5

Although this is a simplified model of deposition rate, it provided the means for achieving one of the objectives of this study, which was to compare the variation of these nebulizer delivery systems with the variation identified by Hess et al1 for various nebulizers.

**Volume of Gas Rebreathed by the Patient**

Testing was performed using the previously described setup (see Fig. 5). Exhalation flow was simulated using 100% oxygen. Nebulizers were run without fluids at 6 L/min, using compressed air. Measurements were taken with an oxygen sensor inside a two-liter bag. The two-liter bag was used to capture two complete inhalations from the outlet of the vacuum source, and the increase in oxygen concentration above ambient was used to calculate the volume of gas rebreathed. The volume of gas rebreathed with the simulated patient breathing directly into ambient conditions was subtracted from the volume of gas rebreathed with each nebulizer delivery system to obtain a final result. The technique was checked using a known dead space of 60 mL, and the volume of gas rebreathed was determined to be 56.5 mL, which was considered to be in good agreement.

**Statistical Analysis**

Summary statistics are reported as mean ± standard error. Differences between groups were determined by one-tailed or two-tailed tests, as appropriate. Statistical significance was set at p < 0.05.

**Results**

**Quantity of Medication Delivered and Treatment Time**

Figure 6 shows the quantity of medication delivered by each nebulizer delivery system. The Vixone nebulizer equipped in the traditional manner delivered 0.53 ± 0.03 mg. The Circulaire delivered 0.32 ± 0.01 mg, which was significantly less than the nebulizer T-piece with corrugated tubing (p < 0.001). During testing it was observed that the Circulaire retained a pool of medication proximal to an internal one-way valve. Further testing was performed on the medication retained proximal to the one-way valve, and it was found to contain a mean 0.62 ± 0.05 mg of albuterol. The AeroTee delivered 0.80 ± 0.02 mg, which was significantly more than the Circulaire or the nebulizer T-piece with corrugated tubing (p < 0.001). The nebulizer T-piece with corrugated tubing treatment time was not significantly different than the Circulaire (p = 0.81) or the AeroTee (p = 0.84) (Fig. 7).
Aerodynamic Particle Size Evaluation

Figure 8 shows the measured MMAD for the three systems. The nebulizer T-piece with corrugated tubing and the AeroTee had MMADs of 2.9 ± 0.2 μm and 3.0 ± 0.2 μm, respectively, and the difference was not significant (p > 0.82). The MMAD of the Circulaire was measured to be 0.7 ± 0.1 μm and found to be significantly less than either the nebulizer T-piece with corrugated tubing (p < 0.001) or the AeroTee (p < 0.001).

Percent of Aerosol Delivered in the 1–5 μm Range

Figure 9 shows the percent of aerosol in the 1–5 μm range. The percent of aerosol in the 1–5 μm range for the nebulizer T-piece with corrugated tubing and the AeroTee were 44 ± 2.5% and 48 ± 2.0%, respectively, and the difference was significant (p = 0.024). The percent of aerosol in the 1–5 μm range for the Circulaire was 24 ± 1.7%, which was significantly less than that of the nebulizer T-piece with corrugated tubing or the AeroTee (p < 0.001).

Mass of Aerosol in the 1–5 μm Range

Figure 10 shows the mass of aerosol in the 1–5 μm range for each nebulizer delivery system. The AeroTee delivered 0.38 ± 0.01 mg of aerosol in the 1–5 μm range, which was more than the nebulizer T-piece with corrugated tubing or the Circulaire (p < 0.001). The nebulizer T-piece with corrugated tubing delivered 0.24 ± 0.02 mg of aerosol in the 1–5 μm range, whereas the Circulaire delivered only 0.08 ± 0.01 mg. The difference between all devices was significant (p < 0.001).

Volume of Rebreathed Gas Evaluation

Figure 11 shows the volumes of gas rebreathed by the simulated patient. The AeroTee and the nebulizer T-piece
with corrugated tubing were measured to have rebreathed volumes of 47.9 ± 3.5 mL/breath and 47.7 ± 3.1 mL/breath, respectively. The difference was not significant (p = 0.93). The volume of rebreathed gas for the Circulaire was 15.3 ± 3.4 mL/breath, which was significantly less than the AeroTee (p < 0.001) or the nebulizer T-piece with corrugated tubing (p < 0.001).

**Discussion**

This study found that the nebulizer delivery system used to deliver aerosolized medication can have a significant effect on the amount and quality of aerosol delivered to the patient. Most noteworthy is how much the AeroTee and Circulaire appear similar from casual observation, and yet the performance of each was strikingly different. The AeroTee, when used with the Vixone nebulizer, was shown to deliver almost 5 times the mass of 1–5 μm-range aerosol as the Circulaire, despite the fact that both are equipped with identical aerosol storage means. Furthermore, the MMAD of the AeroTee, when used with the Vixone nebulizer, was strikingly different than that of the Circulaire. Particularly noteworthy was the finding that the percent difference in the mass of aerosol in the 1–5 μm range and MMAD between the AeroTee and the Circulaire when used with identical nebulizers was larger than the difference for any two of the 17 nebulizers studied by Hess et al.1

The Vixone nebulizer equipped in the traditional manner delivered 0.53 ± 0.03 mg of albuterol, compared to 0.75 ± 0.02 mg as measured by Hess et al. In their study, Hess et al.1 used a sinusoidal waveform to simulate patient breathing that had an I:E of 1:1.5, compared to the I:E of 1:2 simulated in the present study. It is reasonable to expect an increase in inspiratory time to cause an increase in quantity of medication delivered, because less aerosol would be wasted during exhalation. When corrected for the difference in I:E, the results of Hess et al.1 and the results of this study vary only by 14.7%.

The smaller particle size of the Circulaire was a key factor in the dramatically lower mass of aerosol in the 1–5 μm range (see Fig. 5). The MMAD of 0.7 ± 0.1 μm measured in this study is not much different than the MMAD of 0.51 μm reported by the manufacturer of the Circulaire. The mass of aerosol in the 1–5 μm range is an important parameter because it represents the range of particle sizes most likely to deposit in the bronchial airways. Raabe et al.,2,3 in addition to defining a respirable range of aerosol particle sizes as 1–5 μm, also published data showing that the pulmonary (alveolar) deposition fraction for 0.7 μm and 3.0 μm particles is 0.2 and 0.7, respectively. Although there is some deposition for submicron particles, the rate of deposition is three times less than for particles in the peak respirable range.

Several clinical studies have compared the Circulaire to a conventional nebulizer configuration, and all reported equal or slightly greater clinical effectiveness with the Circulaire.2,6–8 Those clinical evaluations would seem to contradict the results of this study. However, in none of those studies was the Circulaire delivery system evaluated separately from the nebulizer used, because in each case the Circulaire with a Vixone nebulizer was compared to a traditional configuration using an Airlife Misty-Neb (Baxter Healthcare, Valencia, California). Hess et al.1 found that the Airlife Misty-Neb produces approximately half as much 1–5 μm range aerosol as the Vixone. A more objective clinical evaluation of the Circulaire would have been performed had both nebulizer delivery systems been equipped with the same brand of nebulizer.

**Conclusions**

Nebulizer delivery systems have at least as great an effect on the quantity and quality of aerosol delivered to the patient as do the individual nebulizers themselves. In
this bench study, the AeroTee delivered superior performance, compared to a nebulizer T-piece with corrugated tubing, whereas the Circulaire, which is similar in form to the AeroTee, delivered less medication than a nebulizer T-piece with corrugated tubing. Further clinical research should be performed on these and other nebulizer delivery systems. When comparing different nebulizer delivery systems, it is important to conduct the work under reasonably similar circumstances, using the same or comparable nebulizers and dosing strategies.

REFERENCES