The Role of Dose Volume in Delivering Albuterol Sulfate with a Low Residual Volume Nebulizer

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INTRODUCTION

Rapid, efficient delivery of bronchodilators is important, particularly in the acute care setting. The standard dose volume of 3 mL with 0.083% albuterol sulfate was established for use with standard nebulizers with residual volumes between 0.8 and 2.0 mL (Hess et al., Chest 1998). Aerogen has two low residual nebulizer systems (Aeroneb® Professional Nebulizer System (Aeroneb Pro) and Aeroneb® Go Nebulizer (Aeroneb Go), Figure 1); both incorporate Aerogen's OnQ™ Aerosol Generator.

The OnQ Aerosol Generator is an electronic micropump (Figure 2) with a residual drug volume as low as 1 microliter. Because of the high efficiency of the aerosolization mechanism, and placement of the drug solution in direct contact with the aerosol generator, the nebulizers' medication cup residual is also low (approximately 0.1 mL).

FIGURE 1: THE AERONEB PRO (LEFT) AND AERONEB GO (RIGHT).

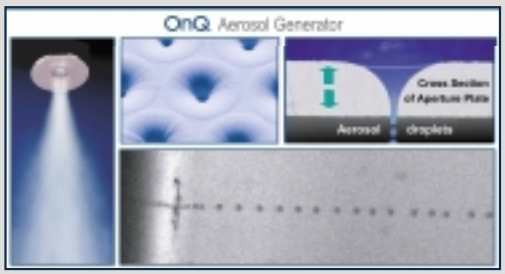

FIGURE 2: THE AEROGEN® ONQ™ AEROSOL GENERATOR (LEFT) WITH A MICROSCOPIC VIEW OF TAPERED APERTURES (UPPER MIDDLE), AND CROSS SECTION OF APERTURES (UPPER RIGHT). HIGH SPEED MICROSCOPIC PHOTOGRAPH OF AEROSOL GENERATED FROM A SINGLE APERTURE (LOWER RIGHT).

OBJECTIVE

We wanted to determine the effect of initial drug volume on inhaled mass and time of administration with these low residual volume nebulizers.

MATERIALS AND METHODS

The two low residual volume nebulizers were studied in a total of three configurations, each aerosolizing 2.5 mg of albuterol sulfate solution in volumes of 3.0 mL (0.083% solution) and 0.5 mL (0.5% solution). The Aeroneb Pro was tested with a standard mouthpiece, and separately with a mouthpiece plus a double one-way valve system and expiratory filter. A prototype of the Aeroneb Go with a mouthpiece was also tested.

Aerosol was delivered to an absolute filter placed between the mouthpiece of the nebulizer and a breath simulator (Hans Rudolph) set to adult breathing parameters (tidal volume 500 mL, rate 15 b/min and inhalation time 35%). (Figure 3).

Drug was eluted from the filter, assayed by HPLC, and expressed as percent of total dose (mean ± SD, n=3). Each experiment was performed in triplicate.

FIGURE 3: MODEL USED FOR MEASURING AEROSOL DELIVERY WITH SIMULATED ADULT BREATHING PATTERN. SHOWN WITH AERONEB PRO WITH DOUBLE ONE-WAY VALVE SYSTEM.

RESULTS

The inhaled mass and treatment time for administration of a single dose of 3.0 mL (0.083% solution), and 0.5 mL (0.5% solution) are shown for the Aeroneb Pro with a standard mouthpiece in Table 1 and with the valve system and filter in Table 2. Data for the Aeroneb Go prototype are shown in Table 3. Inhaled mass is expressed as the actual amount of drug deposited on the filter and as the percentage of initial dose. All reported values are mean ± SD, n=3.

Dose Volume	Inhaled Mass µg	Inhaled Mass % of Dose	Treatment Time (min)
3.0 mL	575 ± 23 µg	23 ± 1%	7 min, 8 s ± 17 s
0.5 mL	540 ± 29µg	22 ± 1%	1 min, 24 s ± 10 s

TABLE 1: TESTING RESULTS FOR THE AERONEB PRO WITH THE SAME DOSE (2.5 MG) OF ALBUTEROL SULFATE ADMINISTERED IN DOSE VOLUMES OF 3.0 ML AND 0.5 ML. DATA ARE MEAN ± SD.

RESULTS (CONT)

Dose Volume	Inhaled Mass µg	Inhaled Mass % of Dose	Treatment Time (min)
3.0 mL	875 ± 39 µg	35 ± 2%	7 min, 1 s ± 13 s
0.5 mL	800 ± 47 µg	32 ± 2%	1 min, 22 s ± 9 s

TABLE 2: RESULTS FOR THE AERONEB PRO WITH VALVE SYSTEM AND FILTER WITH THE SAME DOSE (2.5 MG) OF ALBUTEROL SULFATE ADMINISTERED IN DOSE VOLUMES OF 3.0 ML AND 0.5 ML. DATA ARE MEAN ± SD.

Dose Volume	Inhaled Mass µg	Inhaled Mass % of Dose	Treatment Time (min)
3.0 mL	1084 ± 94 µg	43 ± 4%	6 min, 22 s ± 28 s
0.5 mL	1123 ± 42 µg	45 ± 1%	1 min, 20 s ± 8 s

TABLE 3: TESTING RESULTS FOR THE PROTOTYPE AERONEB GO WITH THE SAME DOSE (2.5 MG) OF ALBUTEROL SULFATE ADMINISTERED IN DOSE VOLUMES OF 3.0 ML AND 0.5 ML. DATA ARE MEAN ± SD.

SUMMARY

Although there was a difference in inhaled mass between nebulizer types, we found relatively no difference in inhaled mass for any nebulizer between the two dose volumes. As expected, the treatment time was substantially shorter with the 0.5 mL dose volume. Reduced treatment time is desirable, particularly in the treatment of acute exacerbation of asthma or COPD. Although comparable inhaled mass can be delivered with shorter treatment time, it is unclear whether the drug concentrations make a difference in airway response.

When using these low residual volume nebulizers there is no significant difference in inhaled mass of albuterol sulfate between 3.0 and 0.5 mL doses, which contain the same drug content. This contrasts with the changes in efficiency with changing dose volumes reported for other small volume nebulizers. There was greater than four fold decrease in the administration time required for the smaller dose volume with the Aeroneb Pro in both configurations and the Aeroneb Go.

CONCLUSION

The Aeroneb Pro and the Aeroneb Go are low residual volume nebulizers; they deliver the same inhaled mass over a range of dose volumes. Use of a lower volume higher concentration solution can reduce the time required for dose administration.

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