COMPARISON OF A NEBULIZER USING A NOVEL AEROSOL GENERATOR WITH A STANDARD ULTRASONIC NEBULIZER DESIGNED FOR USE DURING MECHANICAL VENTILATION

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As presented at American Thoracic Society 97th International Conference • May 2001 • San Francisco, California
ABSTRACT

Ultrasonic nebulizers (USNs) generate aerosols without changing ventilator volumes or alarms. However, USN output varies with gas flow, is position dependent and generates heat. We wanted to determine whether the Aeroneb™ Professional Nebulizer System (Aeroneb Pro; Aerogen, Inc., Sunnyvale, CA)* has similar limitations.

METHODS: We compared performance of the SUN 145 (Siemens-Elema AB, Solna, Sweden) and the Aeroneb Pro operated with 0.083% albuterol sulfate, in both upright and inverted orientation. Mass mean aerodynamic diameter (MMAD) was determined by cascade impaction. Emitted aerosol output and residual volume were determined at flows of 6, 30 and 60 L/min through each nebulizer (n=3). A digital thermistor placed in the medication reservoir monitored changes in temperature.

RESULTS: Output from the SUN 145 varied between 0.18 ± 0.02 (mean ± SE), 0.40 ± 0.05, and 0.56 ± 0.1 mL/min at 6, 30 and 60 L/min, respectively (p < 0.01; ANOVA) in the upright position, with no aerosol generated in the inverted position. In contrast, the Aeroneb Pro had a mean output of 0.35 ± 0.03 mL/min in the plume up (AG up) position at 6, 30 and 60 L/min , increasing to a mean of 0.41 ± 0.05 mL/min (p < 0.05) when plume down. The MMAD (4.1 µm) and residual volume (0.8 mL) were greater with the SUN 145 than the Aeroneb Pro (3.5 µm and 0.2 mL, respectively; p < 0.05 for both). A greater increase (or fluctuation) in temperature from baseline was observed with the SUN 145 (24 ± 3°C) than the Aeroneb Pro (2 ± 1°C; p < 0.01).

SUMMARY: Unlike the standard ultrasonic nebulizer, the Aeroneb Pro operated in both plume up and plume down orientation did not exhibit flow dependent output and did not significantly heat the medication.

CONCLUSION: The Aeroneb Pro provided more consistent aerosol output than the ultrasonic nebulizer.

BACKGROUND

A novel nebulizer designed for use with mechanical ventilators in either a vertical or inverted orientation was evaluated utilizing Aerogen’s aerosol generator (AG). The AG contains a domed aperture plate with precision-formed holes of a discrete shape and size. A vibrational element uses a micro-pumping action to create a fine particle, low-velocity aerosol using no propellants or compressors. Particle size, flow rate and fine particle fraction are functions of the aperture hole exit diameter. We wanted to determine whether the novel nebulizer has similar limitations to the USN.

BACKGROUND (cont.)

During mechanical ventilation, ultrasonic nebulizers (USNs) have the advantage of generating a high aerosol output without changing the volumes or pressures in the ventilator circuit. USNs apply high frequency vibration through a liquid couplant to medication solutions, creating standing waves that generate aerosol particles. Unfortunately, USNs are relatively bulky, position sensitive (recommended to operate within 15° of vertical), and generate considerable heat during operation. In addition, aerosol output varies with the inspiratory flow rate through the nebulizer.
METHODS

Performance of the Aeroneb Pro was compared with that of a Siemens Ultra Nebulizer 145 (SUN 145) ultrasonic nebulizer designed for use with mechanical ventilators.

OUTPUT

Aerosol output (mL/min) was determined by gravimetric analysis with a measured flow of air through the nebulizer T-piece at 6, 30 and 60 L/min. Measurements were made over time, with medication volumes decreasing from 10 to 1 mL at 6 and 30 L/min.

RESIDUAL VOLUME

Residual medication left in the medication cup after nebulization was determined gravimetrically.

AEROSOL CHARACTERISTICS

The mass mean aerodynamic diameter (MMAD) was determined for each nebulizer with albuterol sulfate, using an Anderson Mk II cascade impactor (Anderson Graesby, GA). Volumetric median diameter (VMD), Geometric standard deviation (GSD) and fine particle fraction in the 1-7 µm range (FPF) were determined by laser diffraction with the Spraytech™ (Malvern / INSITEC, San Ramon CA).

TEMPERATURE CHANGES

To determine medication temperature changes during use, both nebulizers were operated with 10 mL of solution, beginning with an ambient temperature of 23 ± 1°C, monitored with a digital thermistor placed in the medication reservoir. The nebulizers were placed between the inspiratory limb and the wye of a standard ventilator circuit, set to standard adult parameters. Temperature of the solution was determined prior to and during operation of the nebulizers at two minute intervals until the reservoir was empty.

RESULTS

OUTPUT

Output from the SUN 145 was 0.18 ± 0.02 (mean ± SE), 0.40 ± 0.05, and 0.56 ± 0.1 mL/min at 6, 30 and 60 L/min, respectively (p < 0.01; ANOVA) in the upright position, with no aerosol generated in the inverted position. In contrast, output of the Aeroneb Pro had a mean of 0.35 ± 0.03 mL/min at 6, 30 and 60 L/min in the plume up position, increasing to a mean of 0.41 ± 0.05 mL/min (p < 0.05) when plume down.

Changes in aerosol output with changes in medication volume in the reservoir measured for both nebulizers at flow rates of 6 and 30 L/min are shown in Figure 6. Changes in output varied dramatically with the SUN 145 with changes in both medication volume and flow rates, while the output of the Aeroneb Pro was consistent throughout.
RESULTS (cont.)

RESIDUAL VOLUME

The amount of residual medication remaining in the nebulizer after nebulization was complete ranged from 0.2-0.4 mL for the Aeroneb Pro nebulizer and 0.8-1.2 mL for the SUN 145.

![Graph: Variance in Aerosol Output with Gas Flow and Medication Volume]

Figure 6: Variation in aerosol output with gas flow and medication volume

CHANGE IN VENTILATOR PARAMETERS

During mechanical ventilation, no detectable changes in delivered pressures or volumes with either nebulizer were observed.

AEROSOL CHARACTERISTICS

AEROSOL DELIVERY DURING MECHANICAL VENTILATION

The amount of albuterol sulfate (0.083%) delivered through a standard ventilator circuit, with an active heated humidifier to the distal end of an endotracheal tube (8.0 mm ID for adult, 3.0 mm ID for neonatal) is shown below (Table 2) as mg of albuterol and the % of nominal dose (% dose).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Peak Flow Rate Range L/min</th>
<th>Rate bpm</th>
<th>Volume mL</th>
<th>Aeroneb Pro µg</th>
<th>% dose</th>
<th>SUN 145 µg</th>
<th>% dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult</td>
<td>60</td>
<td>12</td>
<td>800</td>
<td>315</td>
<td>13</td>
<td>346</td>
<td>14</td>
</tr>
<tr>
<td>Neonatal</td>
<td>6</td>
<td>40</td>
<td>50</td>
<td>87</td>
<td>3.4</td>
<td>68</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 2: Aerosol delivery during mechanical ventilation

![Graph: Medication Temperature/Time]

Figure 7: Medication temperature/time

SUMMARY

While both systems delivered comparable amounts of aerosol to the endotracheal tube during mechanical ventilation, the Aeroneb Pro System provided more consistent aerosol delivery than the SUN 145 at different inspiratory flows in both plume up and plume down positions. The Aeroneb Pro had similar flow and aerosol particle characteristics in both orientations, while the SUN 145 was position dependent. The Aeroneb Pro demonstrated a lower residual volume (0.2-0.4 mL vs. 0.8-1.2 mL), and less heat generation in the medication reservoir over 20 minutes (2 ± 1°C vs. 24 ± 3°C) than the SUN 145.

CONCLUSION

The Aeroneb Pro provides efficient delivery of aerosol during mechanical ventilation without limitations commonly associated with ultrasonic nebulizers.