Using Respirable Drug Delivery Rate (RDDR) to Compare Delivery Efficiency of Three Commercially Available Breath-Enhanced Nebulizers with Budesonide

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INTRODUCTION:
Aerosol characterization is conducted to evaluate nebulizer performance and efficiency. These measures typically include Delivered Dose (DD) upon breath simulation, Mass Median Aerodynamic Diameter (MMAD), Respirable Fraction (RF) and Total Output Rate (TOR). It has since been shown that both Respirable Dose (RD) and Respirable Drug Delivery Rate (RDDR) are also important measures to objectively compare nebulizer efficiency. The aim of this study is to compare in vitro performance and delivery efficiency of 3 commercially available breath-enhanced nebulizers by measuring RD, RDDR, MMAD, and nebulization time with budesonide inhalation suspension (Pulmicort Respules, AstraZeneca, Wilmington, DE).

MATERIALS AND METHODS:
Aerosol particle size distribution was measured with a cooled NGI (Next Generation Impactor, 17°C) at 50% RH and 23°C ambient conditions at a flow rate of 30 l/min. Budesonide inhalation suspension (250μg/mL) with a fill volume of 2.0mL was nebulized in the new LC Sprint Reusable Nebulizer (PARI Respiratory Equipment, Midlothian, VA), the LC PLUS Reusable Nebulizer (PARI), and the Sidestream Plus Reusable Nebulizer (Respironics, Murraysville, PA).

RESULTS:
Table 1:
<table>
<thead>
<tr>
<th>Nebulizer</th>
<th>MMAD [µm]</th>
<th>Nebulization time (spitting +1 min) [min]</th>
<th>RD&lt;5µm [µg]</th>
<th>RDDR [µg/min]</th>
</tr>
</thead>
<tbody>
<tr>
<td>LC SPRINT</td>
<td>5.5</td>
<td>6.0</td>
<td>53.8</td>
<td>49.8</td>
</tr>
<tr>
<td>LC PLUS</td>
<td>5.3</td>
<td>6.0</td>
<td>53.8</td>
<td>49.8</td>
</tr>
<tr>
<td>Sidestream Plus</td>
<td>5.9</td>
<td>6.0</td>
<td>53.8</td>
<td>49.8</td>
</tr>
</tbody>
</table>

RD= Respirable Fraction (RF = %droplets < 5 μm) x Delivered Dose (DD=Drug amount found on both inspiratory filters). RDDR=Respirable Fraction (RF = %droplets < 5 μm) x Drug amount found on first inspiratory filter / 2 minutes.

CONCLUSIONS:
• Of the three nebulizers tested, RDDR was highest with the LC SPRINT Reusable Nebulizer (p<0.002).
• Higher delivery efficiency is associated with potentially shorter nebulization and inhalation times.
• RDDR is 46% higher for the LC SPRINT Reusable Nebulizer compared to the Sidestream Plus nebulizer (p<0.002).
• RD is the same (no significant difference) and RDDR is 25% higher for the PARI LC SPRINT Reusable Nebulizer compared to the LC PLUS Reusable Nebulizer.
• RD and RDDR for the LC PLUS Reusable Nebulizer demonstrate higher delivery efficiency (33% and 39% respectively) compared to the Sidestream Plus nebulizer.
• Treatment time was shortest for the LC SPRINT Reusable Nebulizer, followed by the Sidestream Plus and LC PLUS.
• A higher RDDR indicates more drug delivery to the lower airway per minute.

CLINICAL IMPLICATIONS:
Drug delivery efficiency differs between commercially available nebulizers. Therefore, it is important for clinicians to consider RDDR to ensure patients receive clinically effective doses. The results of these experiments demonstrate that the PARI LC SPRINT Reusable Nebulizer and PARI LC PLUS Reusable Nebulizer deliver more respirable particles of budesonide at a faster rate when compared to the Respironics Sidestream Plus. The PARI LC PLUS Reusable Nebulizer was used in the pivotal clinical trials to prove safety and efficacy for budesonide inhalation suspension (Pulmicort Respules®).

Adherence to aerosol therapy for patients with chronic respiratory disease may be associated with device related factors such as delivery efficiency and speed of treatment. Further investigation is warranted to evaluate the clinical implications of using less efficient nebulizers with current aerosol medications.

References:

Specialist in effective inhalation