Summary

Previous studies compared delivered dose results from a range of nebulizers; one finding was that the AeroEclipse II breath-activated nebulizer (Monaghan Medical Corp., Plattsburgh, NY, USA) produced a higher dose than other jet nebulizers.1,2,3 These studies were performed with simulated adult breathing patterns and the AeroEclipse II nebulizer was used in breath-activated mode. For pediatric and low-flow patient breathing patterns it is required that the nebulizer is switched to continuous mode, as the inhalation flow is insufficient to trigger the breath activation of aerosol generation. In this study we investigated the output of the AeroEclipse II nebulizer in continuous mode, and compared it to a reference breath-enhanced nebulizer, the SideStream Plus nebulizer (Respironics Respiratory Drug Delivery (UK) Ltd, Chichester, UK). The nebulizers were tested with a pediatric facemask (small, disposable AeroEclipse II mask, Monaghan Medical Corp.) and attached to an ASL 5000 breathing simulator (IngMar Medical Ltd, Pittsburgh, PA, USA), which was programmed to reproduce a simulated pediatric breathing pattern (tidal volume = 151 mL, breaths per minute = 25, inhalation:exhalation ratio = 1:1). It was found that, in breath-activated mode, the inhalation flow was, as expected, unable to produce aerosol when a small, disposable AeroEclipse II facemask was used. When used in continuous mode, the AeroEclipse II nebulizer produced a lower emitted dose of salbutamol sulphate (5 mg/2.5 mL, Salamol Steri-Neb, IVAX Pharmaceuticals, West Yorkshire, UK), compared to the breath-enhanced SideStream Plus nebulizer.

Introduction

The manufacturers of the AeroEclipse II breath-activated nebulizer (Monaghan Medical Corp.) highlight the ease of selection for either of the 2 modes of operation (breath-activated or continuous), and propose the use of a facemask with the device, in place of the mouthpiece, if required. They also emphasize that the device “combines high emitted dose with high respirable fraction to deliver high respirable dose to the patient”.4 To achieve the latter requires the patient using the device to be capable of achieving an inspiratory flow of ≥15 L/min, so as to trigger aerosol production in the device.

Owing to their ease of use, and reduced requirement for patient coordination or cooperation, facemasks are commonly used as accessories to jet nebulizers for the administration of aerosol therapy to pediatric asthma patients. The open design of the pediatric facemask used in this study (small, disposable AeroEclipse II mask, PN 65750, Monaghan Medical Corp.), prevents the use of the AeroEclipse II nebulizer in breath-activated mode, as the patient cannot generate sufficient inspiratory flow to open the valve to activate. Hence, continuous mode was used in this study.

The SideStream Plus nebulizer (Respironics Respiratory Drug Delivery (UK) Ltd) was used to provide a reference baseline for the performance of a typical breath-enhanced nebulizer. In this in vitro study, the AeroEclipse II nebulizer and the SideStream Plus nebulizer were characterized in combination with a small, disposable AeroEclipse II facemask and a simulated, sinusoidal, pediatric breathing pattern.

Methods

Emitted dose

A small, disposable AeroEclipse II facemask, with mask connector, was sealed onto a metal faceplate using Parafilm M (Bemis Flexible Packaging, Neenah, WI, USA), and attached to the ASL 5000 breathing simulator (IngMar Medical Ltd). The AeroEclipse II nebulizer and the SideStream Plus nebulizer were characterized as follows: each nebulizer was weighed while empty, then charged with 3 mL of 5 mg/2.5 mL salbutamol sulphate solution (albuterol sulfate; Salamol Steri-Neb, IVAX Pharmaceuticals, West Yorkshire, UK), and then reweighed. Each nebulizer was attached to the faceplate/facemask combination, and the join between the facemask and the faceplate was sealed well with Parafilm M. The breathing simulator was programmed to reproduce a simulated pediatric breathing pattern (tidal volume = 151 mL, breaths per minute = 25, inhalation:exhalation ratio = 1:1). The AeroEclipse II nebulizer was tested in continuous operational mode; an initial test was performed with the AeroEclipse II nebulizer in breath-activated mode, which confirmed that it did not generate aerosol. Nebulizers were operated with a driving medical air flow of 8 L/min, and were run to sputter plus 60 seconds, in accordance with CEN Standard EN 13544-1.5 At the end of the test, treatment times were recorded, and the nebulizers were reweighed. Three examples of each nebulizer type were tested in triplicate (n = 9).
Particle sizing by laser diffraction

Particle sizing by laser diffraction was carried out using a Malvern Spraytec (Malvern Instruments Ltd, Worcestershire, UK). The AeroEclipse II and SideStream Plus nebulizers were each charged with 3 mL of 5 mg/2.5 mL salbutamol sulphate solution and operated using a driving medical air flow of 8 L/min. Extraction air flow through the Malvern Spraytec inhalation insert was set to 30 L/min. Nebulizers were attached to a sealed facemask/faceplate combination and the join between the facemask and faceplate was sealed well with Parafilm M. Nebulizers were tested in triplicate (n = 9). Data were collected for the first 60 seconds of treatment, and were averaged to give the fine particle fraction (FPF; % particles <5 µm) and the mass median diameter (MMD; µm).
Results

Table 1. Nebulization characteristics (n = 9).

<table>
<thead>
<tr>
<th></th>
<th>AeroEclipse II [continuous mode]</th>
<th>SideStream Plus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emitted dose (mg solution)</td>
<td>1568</td>
<td>1801</td>
</tr>
<tr>
<td>Respirable emitted dose (mg solution)</td>
<td>1060</td>
<td>1310</td>
</tr>
<tr>
<td>Treatment time (s)</td>
<td>266</td>
<td>179</td>
</tr>
<tr>
<td>MMD (µm)</td>
<td>3.58</td>
<td>3.26</td>
</tr>
<tr>
<td>FPF (%)</td>
<td>67.6</td>
<td>72.7</td>
</tr>
<tr>
<td>Output rate - emitted dose (mg/min)</td>
<td>354</td>
<td>604</td>
</tr>
</tbody>
</table>

The AeroEclipse II nebulizer delivered a lower emitted dose, produced a lower percentage of particles less than 5 µm in diameter, and yielded a correspondingly lower respirable emitted dose, in a shorter time than the reference breath-enhanced SideStream Plus nebulizer.

Discussion

When used in continuous mode, with a pediatric facemask and a simulated breathing pattern applied, the AeroEclipse II nebulizer delivered a lower emitted dose than the reference SideStream Plus nebulizer. The opposite result was found in previous studies, when the AeroEclipse II nebulizer was operated in breath-activated mode into an adult breathing pattern. 2,3 The results presented here, concerning the delivery of salbutamol sulphate solution, are similar to the results of Berg and Picard, who delivered budesonide into a pediatric breathing pattern. 5 In their study, the emitted dose from the AeroEclipse II nebulizer was approximately 19% lower than the emitted doses from the breath-activated nebulizers tested (the SideStream Plus nebulizer and the LC Plus nebulizer [PARI GmbH, Starnberg, Germany]). An in vivo study by Geller et al reported an expected lung dose that was 27% lower from an AeroEclipse II nebulizer than from a LC Plus nebulizer, when a well-fitting facemask was used. 7 The lower delivered dose from the AeroEclipse II nebulizer into a pediatric breathing pattern does not seem to be drug specific.

Conclusions

Breath-enhanced nebulizers have been used for many years to deliver drugs for inhalation across a wide variety of patient types. Switching to nebulizers with alternate (or dual) modes of operation can result in different doses being delivered. The extent of this difference can vary (either greater or lesser) in different patient groups, and should be understood for each of these groups where changes in dosing are not desired.

References

2. Hatley RHM, Byrne S, and Woodington B. Delivered dose comparison between breath-activated (metered dose and non-metered dose) and breath-enhanced nebulizers. 2013 [Abstract submitted to DDL].