### Introduction

Holding chamber can be defined as a chamber allowing the storage of the aerosol produced in a close volume to limit aerosol leak. Holding chambers do not operate in the same way during inhalation and exhalation phase (in opposition to a spacer). During inhaling phase, ambient air enters the holding chamber, crosses the close volume and transports the aerosol to the patient. During exhalation, exhaled air leaves the holding chamber and does not cross the close volume where the aerosol produced is stored. Available holding chambers are valved holding chamber.

- A new holding chamber has been developed (patent pending) without valve system (VVHC, Atomisor, France).
- This new holding chamber could be disposable.
- The aim of this study was to compare the performances of this new holding chamber for a mesh nebulizer (Aeroneb® Go, Aerogen, USA) to available jet and mesh nebulizers.

### Material and methods

- Pari LC+ jet nebulizer and Eflow rapid breath enhanced mesh nebulizer were loaded with 5ml of solution and VVHC-AeronebGo with 2.5ml of solution. Pari LC+ jet nebulizer and Aeroneb Go standard mesh nebulizer were loaded with 2ml of suspension and VVHC-AeronebGo (Figure 1) with 1ml of suspension.

- Particle size was measured with a laser diffraction method (Mastersizer X, Malvern, UK) (Figure 2).

- Inhalable fraction was measured by a filtering method. A breath simulator (Harvard Apparatus) was setup in accordance with the European Standard (500ml, 1/1, 15/min).

- Aerosol was collected on absolute filters placed at the mouthpiece (inhaled mass) (Figure 3). Inhaled mass was calculated by the residual gravimetric method (1) which weights the filters both before and after aerosol collection and filter drying corrected by the proportion of drug contained in total mass. Inhaled volume was calculated by the ratio between inhaled mass and the drug concentration.

- Nebulization time was determined one minute after sputtering for jet nebulizer and at the end of complete aerosol generation for mesh nebulizers.

### Results

<table>
<thead>
<tr>
<th>Nebulizer/drug</th>
<th>Inhaled fraction</th>
<th>Inhalable volume (µl)</th>
<th>VMD (µm)</th>
<th>Time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pari LC+ /solution (5ml)</td>
<td>40% ± 2%</td>
<td>2021 ± 99</td>
<td>4.0 ± 0.2</td>
<td>12.9 ± 0.9</td>
</tr>
<tr>
<td>Eflowrapid /solution (5ml)</td>
<td>38% ± 3%</td>
<td>1917 ± 141</td>
<td>4.5 ± 0.1</td>
<td>7.0 ± 1.0</td>
</tr>
<tr>
<td>Aeroneb Go + VVHC/solution (2.5ml)</td>
<td>77% ± 6%</td>
<td>1935 ± 149</td>
<td>4.6 ± 0.2</td>
<td>8.2 ± 0.5</td>
</tr>
<tr>
<td>Pari LC+ / suspension (2ml)</td>
<td>36% ± 5%</td>
<td>762 ± 95</td>
<td>4.6 ± 0.2</td>
<td>5.0 ± 0.3</td>
</tr>
<tr>
<td>Aeroneb Go / suspension (2ml)</td>
<td>37% ± 8%</td>
<td>749 ± 43</td>
<td>4.6 ± 0.5</td>
<td>6.2 ± 0.6</td>
</tr>
<tr>
<td>Pari LC+ / suspension (1ml)</td>
<td>37% ± 8%</td>
<td>785 ± 67</td>
<td>4.2 ± 0.2</td>
<td>3.6 ± 0.2</td>
</tr>
</tbody>
</table>

Table 1: In vitro results of nebulizers performances with a solution and a suspension (n=6 for each result)

- Results detailed in the table 1 show that nebulizers produced a volume mean diameter (VMD) range from 4.0 to 4.6 µm. Aeroneb go with VVHC produces a VMD range from 4.2 µm to 4.6 µm. 
- A statistical difference was obtained in terms of inhalated fraction between nebulizers for each drug (p<0.001, n=18) and no statistical differences in terms of inhalable volume (p>0.5, n=18). Aeroneb go with VVHC offers a two-fold increase in inhalable fraction in comparison to the others tested nebulizers without modifying inhalable volume. 
- Breath enhanced mesh nebulizers (Eflow rapid and Aeroneb Go with VVHC) decrease the nebulization time in comparison with jet nebulizer (Pari LC+) and standard mesh nebulizer (Aeroneb Go).

### Conclusion

The new accessory (VVHC) for Aeroneb Go nebulizer offers a two-fold increase in inhalable fraction in comparison to a jet and mesh nebulizers, allowing use of 50% less drug without modifying inhalable volume for treatment.


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