Effect of spacer volume on drug delivery using mechanical ventilation: An in vitro study.

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Introduction

The effectiveness of aerosol delivery during mechanical ventilation is influenced by many factors which could be related to the patient, ventilator or the inhaler device [1]. The influence of parameters related to the spacer such as its type, material, geometrical shape, position on the circuit and internal volume has an impact on aerosol delivery [2-3]. The aim of this study was to evaluate the influence of the internal volume of prototypes spacers on the in vitro drug delivery of formulations delivered by a pressurized dose metered (pMDI) and a vibrating mesh nebulizer (VMN) in an adult mechanical ventilation model. The performance of four different spacers with the same geometrical shape and same material but different internal volumes were studied at two different positions in the mechanical ventilation circuit, before and after the Y piece.

Material and methods

A ventilator (Evita 2 Dura, Dräger) was used in volume controlled mode (Vt = 450 mL, f = 15 cycles/min, Positive End Expiratory Pressure (PEEP) = 5 cmH_2O, ratio between inspiratory and expiratory time = ½ and a flow rate of 21 L/min) connected to the test lung model (SmartLung Adult, IMT Medical : Resistance = 5 mbar/L/s and Compliance = 30 mL/mbar) as described in figure 2.

A 7.5 mm endotracheal tube (ETT) and a right-angle elbow adapter were inserted between the Y-piece and the Test Lung. The prototypes were inserted in two different positions : 1) in the inspiratory limb (before Y piece) and between the Y piece and the right-angle elbow (after the Y piece). The delivered dose was collected on a filter inserted between the ETT and the test lung model.

Two different measurements were performed :

- Use with a pMDI : 10 doses containing 100 µg of Salbutamol (Ventolin® 100 µg, GlaxoSmithKline) were actuated in the prototypes during inspiration.
- Use with a vibrating mesh nebulizer : A solution containing 5 mg of Salbutamol (Salbutamol Mylan, 2,5 mg/2,5 mL) was nebulized with the vibrating mesh nebulizer Aeroneb® Pro (Aerogen).

The filter and each component of the mechanical ventilation circuit were recovered with a NaCl solution (0,1 M) and quantified by UV spectrophotometry. Each measurement was performed three times. Results are expressed as means ± standard deviation.

Statistical analyses were performed using GraphPad Prism 6,01 (GraphPad Software, CA) and consisted of one way ANOVA and multiple t-tests. A p-value < 0,05 was considered significant.

Conclusion

Results showed that the larger was the spacer volume the higher was the drug delivered by a pMDI and nebulizer when the device is located in the inspiratory limb before the Y piece.

Results obtained with the spacer inserted after Y piece showed that the spacer volume had an influence on the drug delivered by a pMDI, but the spacer volume shows to have no impact on the drug deposition by a vibrating mesh nebulizer in this considered volume range.

References

1 : Ari A, Fink JB: Factors affecting bronchodilator delivery in mechanically ventilated adults, *Nurs Crit Care* 2010, 15:192-203.

2: Diot P, Morra L, Smaldone GC: Albuterol delivery in a model of mechanical ventilation. Comparison of metered dose inhaler and nebulizer efficiency, *Am J Respir Crit Care Med* 1995, 4.

3: Ari A, Atalay OT, Fink JB: Evaluation of Aerosol Generator devices at 3 Locations in Humidified and non humidified Circuits During Adult Mechanical Ventilation, *Respir care* 2010, 55:837-844.

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Prototypes

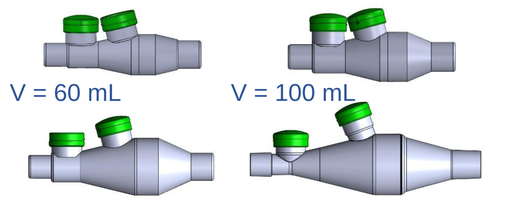


Fig 1: Drawings of the four prototypes with different volumes (Solidworks, France)

CombiHaler® spacer (Laboratoire OptimHal, Valognes, France) has an internal volume of 210 mL. Three prototypes with different volumes (150 mL, 100 mL and 60 mL) and the same geometrical shape of the CombiHaler® were created with Solidworks (Dassault System) and 3D printed with a PLA material. To avoid any additional effect of the material on the drug deposition, CombiHaler® was 3D printed with the same material than the prototypes.

In vitro Aerosol delivery

Before Y piece

After Y piece

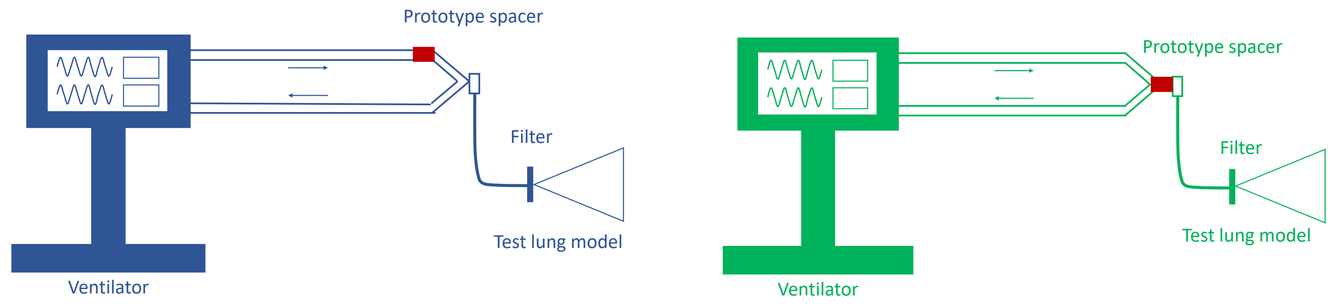
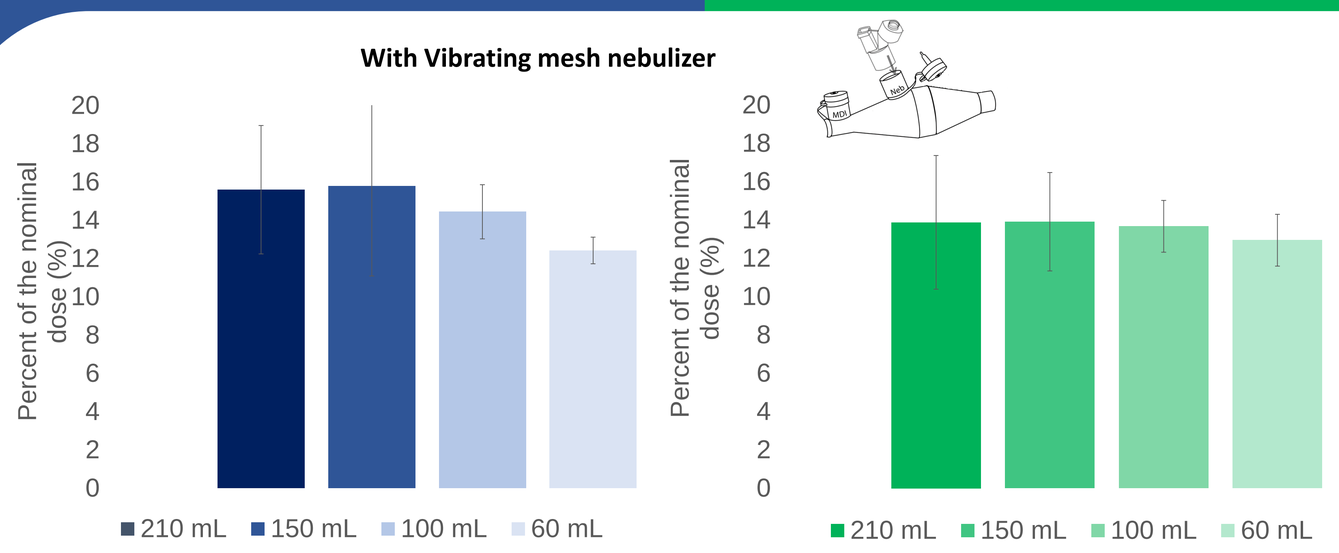


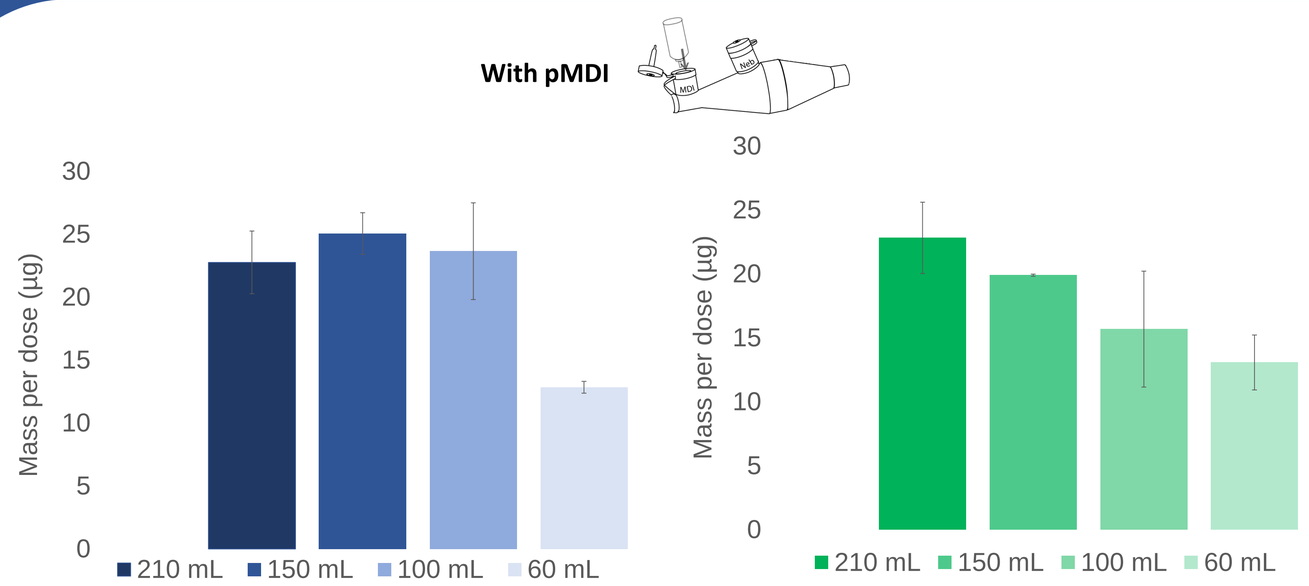
Fig 2: Schematic drawing of the bench model used for the experiments with the prototype inserted before the Y piece (left) and after the Y piece (right).



Percent of the nominal dose (%) obtained on the filter for the prototypes when located before (left) or after the Y piece (right) when using with the nebulizer.

The drug collected on the filter with the VMN shows a significant decrease for the smaller device (p-value < 0,05).

No significant influence on drug recovery with the VMN is observed for the four spacers (p-value > 0,05).



Mass per dose (µg) obtained on the filter for the prototypes when located before (left) or after the Y piece (right) when using with the pMDI.

The drug collected on the filter with pMDI show a significant decrease for the smaller device (p-value < 0,05).

The drug collected on the filter with pMDI show a steadfast decrease with decreasing volume (p-value < 0,05).