In vitro evaluation of a new spacer with Respimat® in mechanical ventilation.

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Introduction

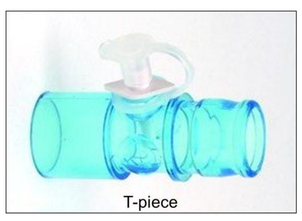
The factors influencing aerosol delivery in mechanical conditions relate to the ventilator, the ventilation circuit and the device used to administer inhaled medication. Use of a spacer would appear therefore as a way to optimize aerosol delivery in mechanical ventilations, both with MDIs and mesh nebulizers. A new spacer suitable for either a pMDI or a mesh nebulizer has been specifically designed for circuits of invasive mechanical ventilation.

The purpose of this study was to evaluate the mass and the particle size of tiotropium delivered by Respimat® using a spacer named Combihaler in a model of adult mechanical ventilation.

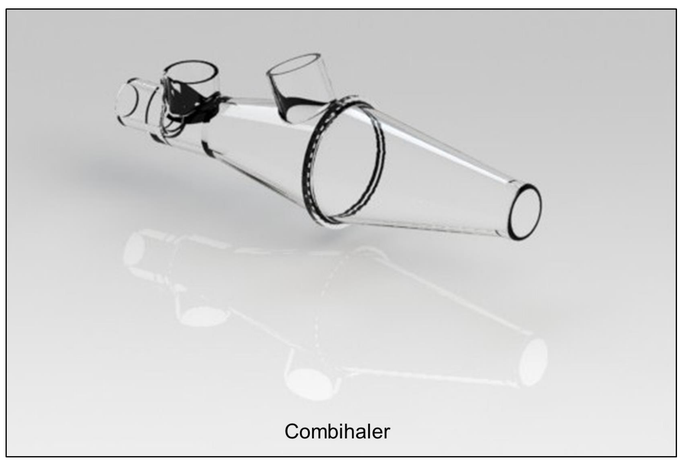
• In this study, Spiriva® Respimat® 2.5 µg per dose (Boehringer Ingelheim, France) was used with two devices:

- T-piece (Allegiance Healthcare Corporation, USA)
- Combihaler spacer (Protec'Som, France)

Spiriva Respimat



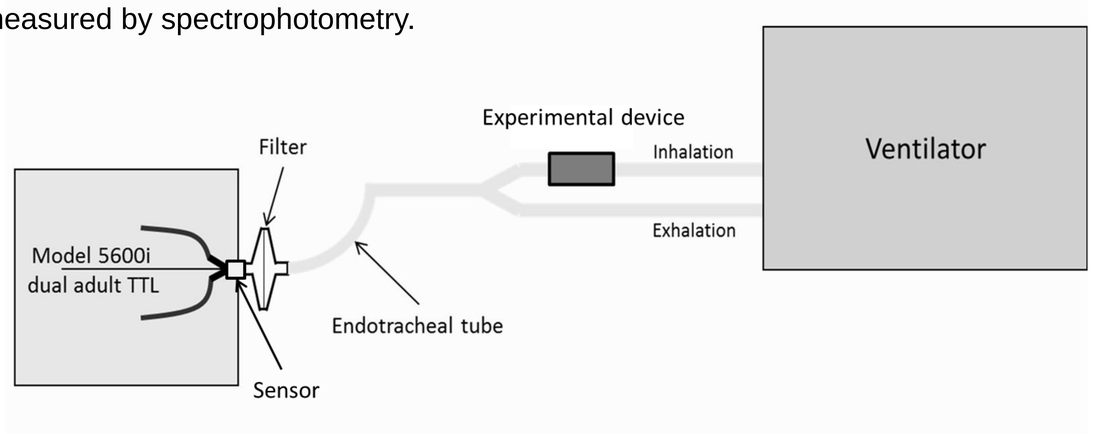
T-piece



Combihaler

• According to the European Pharmacopoeia, particle size delivered by Respimat® was measured using a cascade impactor NGI (Next Generation Impactor, MSP, USA) at 30 L/min.

• To evaluate the drug delivery by Combihaler spacer in mechanical ventilation, the experimental set up assembly includes a respirator (Volume controlled, Vc = 450 mL, f = 15/min, PEEP = 6, P max = 19, Ti / Ttot = 40/60) and a model of adult lung Dual TTL 5600i (Michigan Instruments). A 7.5 mm endotracheal tube and a right-angle elbow adapter were used. An absolute filter (Gelman, Ann Arbor, Michigan, USA) was placed between the extremity of the endotracheal tube and the lung model to filter the aerosol delivery to the lung model. The influence of the time of delivery has been studied: actuation at the beginning of the inspiratory phase and actuation at the beginning of the expiratory phase. Inhalable tiotropium deposited on filter was measured by spectrophotometry.



• A filter was placed after the endotracheal tube to measure the delivered aerosol.

• Statistical analyses were performed using GraphPad Prism 5.01 (GraphPad Software, San Diego, CA) and consisted of a two-way ANOVA and t tests. Six measurements were made for each set-up. For all tests, $p < 0.05$ was considered significant..

Figure 1: Calibration curve for the tiotropium.

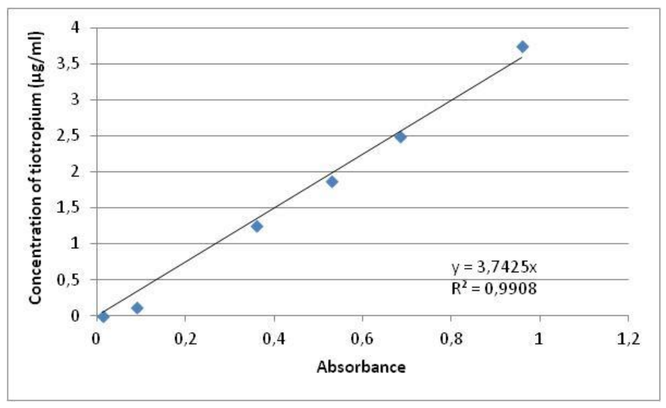
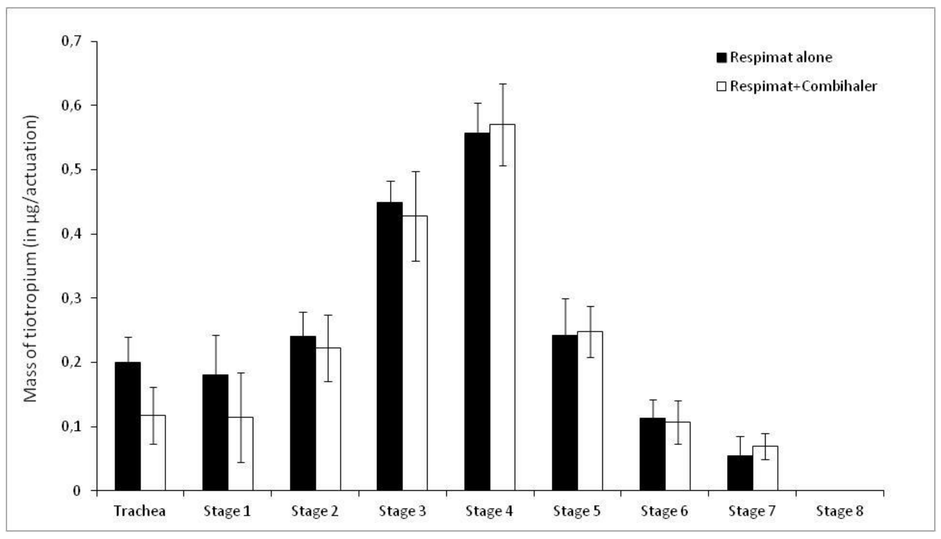


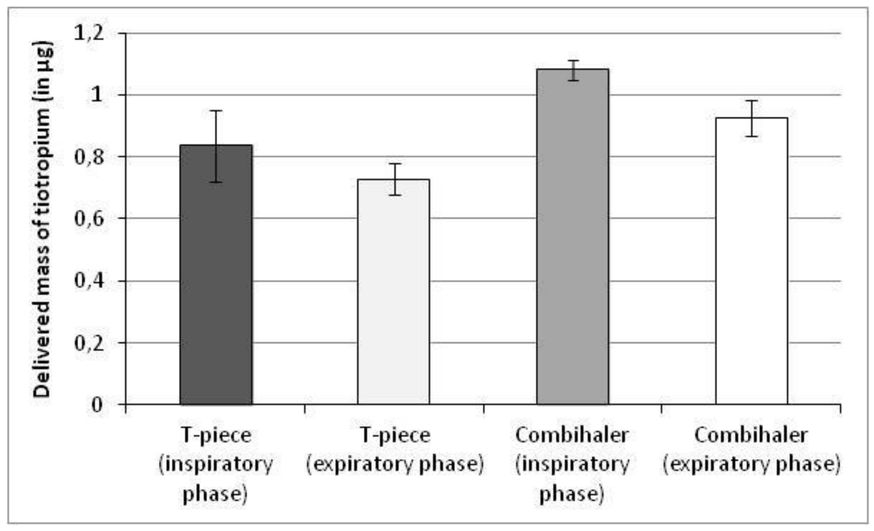
Figure 2: Tiotropium mass distribution (Mean ± SD) in the NGI impactor per actuation.



Based on the the cascade impactor measurement, the MMAD is:
1.4 µm ± 0.02 with the Combihaler
1.6 µm ± 0.03 without the Combihaler.

The fine particle mass is:
1.42 ± 0.20 µg with the Combihaler
1.41 µg ± 0.18 µg without the combihaler

Figure 3: Delivered mass of tiotropium (Mean ± SD) with the actuation of Respimat® during the inspiratory phase or during the expiratory phase.



Based on the mechanical ventilation experiments, the inhalable mass of tiotropium is:

1.08 ± 0.03 µg during the inspiratory phase
0.92 ± 0.05 µg during the expiratory phase

Conclusion

In conclusion, the Combihaler spacer allows the aerosol administration by the Respimat device in mechanical ventilation conditions and doesn't modify the performance of Respimat device with the cascade impactor. A small difference was obtained between the actuation during the inspiratory phase and the expiratory phase in mechanical ventilation.