Abstract

Background: Combining oxygen-therapy with aerosol delivery within High-flow-nasal-cannula (HFNC) oxygen therapy is an attractive practice. The possibility of such therapeutic combination in the clinical setting is still argued. Delivered dose (DD) was found to decrease with increasing gas flow rates and with smaller sized cannulas. The aim of the present work was to provide *in -vitro* data quantifying amount of aerosol emitted at the cannula outlet using different aerosol generators at low oxygen flow and then estimating the relative *in-vivo* pulmonary and systemic delivery of these aerosol generators in acutely exacerbated chronic obstructive pulmonary disease (COPD) patients receiving oxygen therapy.

Materials, Subjects and Methods: Aerogen-Solo vibrating-mesh (SOLO), jet-nebulizer (JN), Combihaler connected to metered-dose-inhaler (MDI) and SOLO, MDI connected to AeroChamber-Vent (VC) and MDI connected to AeroChamber-Mini (MC) were used to deliver aerosol in HFNC *in-vitro* setting. They were placed downstream from the humidification chamber. DD was salbutamol collected on a filter mounted to breathing simulator adjusted to simulate adult breathing pattern. Particle size distribution was measured by cooled Andersen-cascade-impactor. The *in-vivo* study was a prospective, randomized, open-label trial in a cross over design where COPD patients receiving oxygen by means of HFNC system were randomized to study doses of 5 mg salbutamol nebulized by JN or SOLO with T-adaptor or with Combihaler on day 1, 3 and 5 of admission. Two urine samples were collected from each patient, one was provided 30 min post inhalation (USAL

0.5) and the other was pooled to 24 hr post inhalation (USAL 24). The amount of salbutamol in each collected sample was then determined.

Results: SOLO with its T-piece delivers DD~35% of nebulizer charge with high fine-particle-dose (FPD). Both Combihaler and JN delivered~18% with lower FPD. MDI with both spacers delivers only 2.1 and 1.3% of nominal dose, respectively. Mass-median-aerodynamic-diameters were small for the SOLO, Combihaler and JN and high for the two spacers (VC and MC). Twelve (6 females) patients were included, age 53.7 (8) years. SOLO with T-piece and Combihaler demonstrated the higher USAL 0.5 and USAL 24 post inhalation, compared to ($p<0.01$) JN. No significant different was found between T-piece and Combihaler.

Conclusion: Salbutamol can be delivered efficiently using SOLO, with both T-piece and Combihaler, and jet-nebulizer during oxygen therapy using HFNC system. While MDIs with spacers delivers negligible amounts of salbutamol below that expected for clinical response in the *in- vitro* setting. SOLO with both T-piece and Combihaler have proven to provide higher *in-vivo* pulmonary drug delivery than the traditionally used JN when combined with oxygen-therapy within HFNC circuit.