Using Respirable Drug Delivery Rate (RDDR) to Compare Delivery Efficiency of Three Commercially Available Breath-Enhanced Nebulizers with Budesonide

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INTRODUCTION:

Aerosol characterization is conducted to evaluate nebulizer performance and efficiency. These measures typically include Delivered Dose (DD) upon breath simulation, Mass Median Aerodynamic Diameter (MMAD), Respirable Fraction (RF%) and Total Output Rate (TOR). It has since been shown that both Respirable Dose (RD) and Respirable Drug Delivery Rate (RDDR) are also important measures to objectively compare nebulizer efficiency[1]. The aim of this study is to compare the in-vitro performance and delivery efficiency of 3 commercially available breath-enhanced nebulizers by measuring RD, RDDR, MMAD and nebulization time with budesonide inhalation suspension (Pulmicort Respules, AstraZeneca, Wilmington, DE).

MATERIALS AND METHODS:

Aerosol particle size distribution was measured with a cooled NGI (Next Generation Impactor, 17°C) at 50% RH and 23°C ambient conditions at a flow rate of 30 l/m. Budesonide inhalation suspension (250µg/ml) with a fill volume of 2.0mL was nebulized in the new LC Sprint Reusable Nebulizer (PARI Respiratory Equipment, Midlothian, VA), the LC PLUS Reusable Nebulizer (PARI), and the Sidestream Plus Reusable Nebulizer (Respironics, Murraysville, PA).

Picture 1:
LC SPRINT
Reusable Nebulizer

Picture 2:
LC PLUS
Reusable Nebulizer

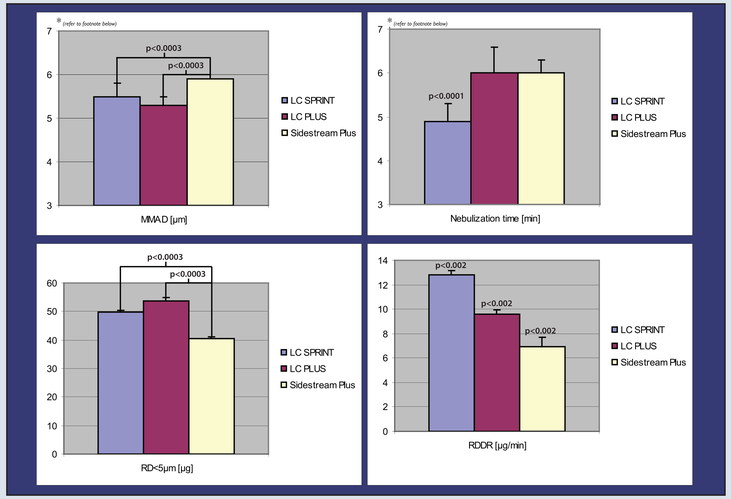
Picture 3:
Sidestream Plus
Reusable Nebulizer

All tests were conducted using a 1.2bar compressed air supply (PARI PRONEB Ultra II USA/PARI BOY EU). Breath simulation was performed with the PARI COMPAS breath simulator using a tidal volume of 500ml, 15 breath/min, I:E ratio 50:50 to investigate nebulization time and DD. The inspiratory filters were exchanged once after 2 minutes. The amount of budesonide found on the inspiratory filters and in the nebulizer residue was assayed from inspiratory filters using a validated internal standard HPLC-UV method.

Respirable Dose (RD) and Respirable Drug Delivery Rate (RDDR) were calculated as follows: RD= Respirable Fraction (RF = %droplets < 5 µm) x Delivered Dose (DD=Drug amount found on both inspiratory filters). RDDR=Respirable Fraction (RF = %droplets < 5 µm) x Drug amount found on first inspiratory filter / 2 minutes.

RESULTS:

Nebulizer	MMAD [µm] Mean	Nebulization time (sputtering +1 min) [min] Mean	RD<5µm [µg] Mean	RDDR [µg/min] Mean
LC SPRINT	5.5	4.9	49.8	12.8
LC PLUS	5.3	6.0	53.8	9.6
Sidestream Plus	5.9	6.0	40.4	6.9



**The Y scale has been adjusted for better clarification of results.*

Table 1: *Aerosol characteristics measured with NGI (17°C) at 50% RH and 23°C ambient conditions at a flow rate of 30 l/m. All tests were conducted using a 1.2bar compressed air supply (PARI PRONEB Ultra II USA/PARI BOY EU) with an inspiratory flow of 15L/min. Breath simulation was performed with the PARI COMPAS breath simulator using a tidal volume of 500ml, 15 breath/min, I:E ratio 50:50.*

CONCLUSIONS:

- Of the three nebulizers tested, RDDR was highest with the LC Sprint Reusable Nebulizer ($p<0.002$). Higher delivery efficiency is associated with potentially shorter nebulization and inhalation times[2].
- RDDR is 46% higher for the LC Sprint Reusable Nebulizer compared to the Sidestream Plus nebulizer ($p<0.002$).
- RD is the same (no significant difference) and RDDR is 25% higher for the PARI LC Sprint Reusable Nebulizer compared to the LC PLUS Reusable Nebulizer.
- RD and RDDR for the LC PLUS Reusable Nebulizer demonstrate higher delivery efficiency (33% and 39% respectively) compared to the Sidestream Plus nebulizer.
- Treatment time was shortest for the LC Sprint Reusable Nebulizer, followed by the Sidestream Plus and LC PLUS.
- A higher RDDR indicates more drug delivery to the lower airway per minute[1].

CLINICAL IMPLICATIONS:

Drug delivery efficiency differs between commercially available nebulizers[3]. Therefore, it is important for clinicians to consider RDDR to ensure patients receive clinically effective doses. The results of these experiments demonstrate that the PARI LC Sprint Reusable Nebulizer and PARI LC PLUS Reusable Nebulizer deliver more respirable particles of budesonide at a faster rate when compared to the Respironics Sidestream Plus. The PARI LC PLUS Reusable Nebulizer was used in the pivotal clinical trials to prove safety and efficacy for budesonide inhalation suspension (Pulmicort Respules®)

Adherence to aerosol therapy for patients with chronic respiratory disease may be associated with device related factors such as delivery efficiency and speed of treatment. Further investigation is warranted to evaluate the clinical implications of using less efficient nebulizers with current aerosol medications.

References:

(1) Keller M et al.: (2002) Respirable Drug Delivery Rate (RDDR) An objective parameter to assess the Efficiency of Nebulizers.; Poster American Thoracic Society.

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(3) Smaldone, G. (1998). In Vitro Determination of Inhaled Mass and Particle Distribution for Budesonide Nebulizing Suspension; Journal of Aerosol Medicine 11: 113-125.

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