INHALED ANTIBIOTIC DELIVERY BY PNEUMATIC NEBULIZATION: CASE STUDY COMPARING BREATH ACTUATED WITH BREATH ENHANCED NEBULIZERS FOR COLISTIMETHATE SODIUM

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BACKGROUND

- Inhaled colistimethate sodium is a polymixin antibiotic that is indicated for treating lung infection with *pseudomonas aeruginosa* in cystic fibrosis
- Although dry powder inhaler-based products are available, this therapeutic agent is often given by pneumatic nebulization
- To ensure optimal dosing, the possibility of using such products in conjunction with a Breath Actuated Nebulizer (BAN) may be of interest, as this type of nebulizer conserves medication during exhalation rather than allowing it to escape and disperse into the local environment
- The present laboratory investigation was designed to evaluate colistimethate sodium output from a BAN configuration able to be used in either the hospital or home environment
- Comparison measurements were also gathered for a continuous Breath Enhanced Nebulizer (BEN), to provide benchmark data

MATERIALS AND METHODS

- BAN group (n=5 devices)
  - ***AeroEclipse****XL with ***Ombra**** Table Top Compressor; AE-XL, Trudell Medical international, London, ON, Canada
- BEN group (n=5 devices)
  - LC Plus† with PARI-BOY† SX compressor; PARI Respiratory equipment, Midlothian, VA, USA

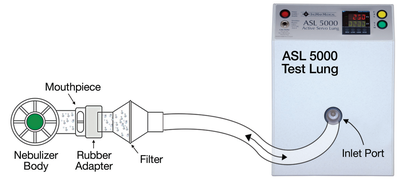
AeroEclipse* XL BAN

Ombra* Table Top Compressor

LC Plus† BEN

PARI Boy† SX
Table Top Compressor

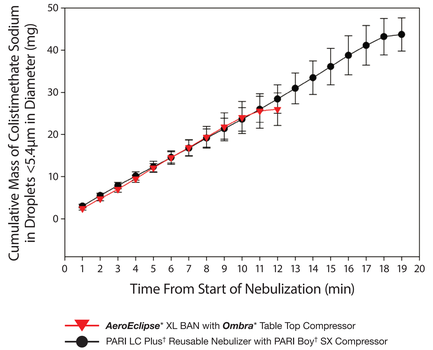
- 4.0 mL fill colistimethate sodium from ampoule
  - Colomycin† for injection, Forest Laboratories UK Ltd.
  - Equivalent to 160 mg colistimethate sodium
  - Representative polymyxin antibiotic (polymyxin E)
- Adult patient tidal-breathing simulation with ASL5000 Test Lung (IngMar Medical, Pittsburgh, PA)
  - Tidal volume = 600 mL
  - Duty cycle = 33%
  - Rate = 10 breathing cycles/min
- Filter collection at mouthpiece of nebulizer at 1-min intervals from start to onset of sputter
  - Colistimethate sodium recovered quantitatively and assayed by HPLC-UV spectrophotometry to determine total mass of colistimathate sodium (*TMcs*) at each time interval



- The BANs were operated in the breath actuated mode for this part of the study
  - Medication is only delivered during the inspiratory portion of each breathing cycle
  - There is negligible waste of medication to the ambient surroundings during exhalation
- The measurements were subsequently repeated with the same nebulizers sampling continuously at 15 L/min to determine droplet size distribution by Next Generation pharmaceutical Impactor (NGI)
  - Fine Droplet Fraction < 5.4 µm diameter ($FDF_{<5.4\ \mu m}$) determined in accordance with USP Chapter 1601 (2013)
- Fine particle mass delivery profiles for colistimethate sodium aerosols were constructed on a minute by minute basis from the product of *TMcs* and $FDF_{<5.4\ \mu m}$

RESULTS

- The figure summarizes the time dependant delivery of colistemethate sodium from BAN and BEN groups as Fine Particles <5.4µm aerodynamic diameter



- Fine particle mass delivery rates during the first 10 minutes from start of nebulization for both BAN and BEN systems were comparable
- This outcome might be anticipated, since both nebulizers operate as breath entrainment devices having similar droplet aerodynamic particle size distributions
- *TM* delivered to sputter was appreciably higher for the ***AeroEclipse****XL BAN

CONCLUSIONS

- Conservation of medication and associated avoidance of environmental losses from fugitive emissions with the BAN nebulizer system was evident by the increased fine particle mass, compared with the BEN nebulizer system
- Mean delivery rates of the therapeutically beneficial fine droplets were, however, comparable at ca. 2.4 mg/min for both nebulizer-compressor systems
- In this particular instance, the caregiver therefore has the option of stopping treatment after 12 minutes with the BAN if a similar dose or run time to the BEN is desired, or can continue to deliver additional dose in the same treatment session if it is considered clinically desirable to maximize delivered dose
- This additional dose is well within the safe and effective daily dose range reported from a colistimethate sodium marketed product registration information[1]

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† Summary of Product Characteristics, Colomycin Injection (Aerosol Inhalation), Forest Laboratories, UK Ltd.

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