DELIVERY OF TOBRAMYCIN VIA PNEUMATIC NEBULIZER: A LABORATORY STUDY COMPARING BREATH ACTUATED AND BREATH ENHANCED DEVICES

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BACKGROUND

- Pneumatic nebulization is the mainstay of care of patients requiring inhaled antibiotic therapy in association with pulmonary diseases such as cystic fibrosis and chronic obstructive pulmonary disease
- Breath Actuated Nebulizers (BANs) offer the opportunity to provide such therapy without release of fugitive emissions to caregivers during exhalation, as well as conserving medication if the patient chooses to interrupt therapy
- This bench study was undertaken to determine the delivery of tobramycin using a BAN, with data from a Breath Enhanced Nebulizer (BEN) as a benchmark

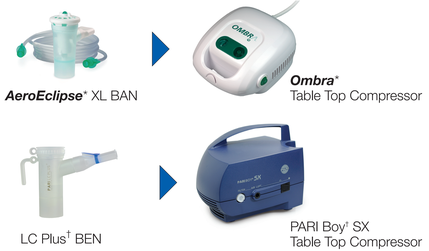
MATERIALS AND METHODS

BAN group (*n*=5 devices)

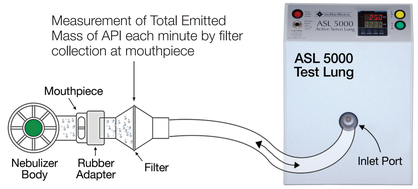
- ***AeroEclipse**** XL with ***Ombra**** Table Top Compressor (AE XL BAN/compressor)
  - Trudell Medical international, London, ON, Canada

BEN group (*n*=5 devices)

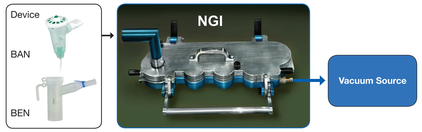
- LC Plus†
  - With PARI-BOY† SX compressor
  - PARI Medical Holding GmbH, Germany



- 5.0-ml fill tobramycin from ampule
  - TOBI†, Novartis Pharmaceuticals Corp, East Hanover, NJ
  - Equivalent to 300 mg tobramycin
  - Representative aminoglycoside antibiotic
- Adult patient tidal-breathing simulation
  - 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
  - Tobramycin recovered quantitatively and assayed by evaporative light scattering (ELS)-HPLC to establish average delivery rate/min (DR)



- 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)



- The mass-weighted rate of delivery of fine droplets < 5.4 µm ($FDM_{<5.4\mu m/min}$) was the principal *in vitro* performance metric, determined as the product of DR_{min} and $FDF_{<5.4\mu m}$
- The total mass of tobramycin delivered (*TM*) was also determined

RESULTS

- The table summarizes the results for DR_{min}, $FDF_{<5.4\mu m}$, $FDM_{<5.4\mu m/min}$ and *TM*

Type	BAN	BEN
Nebulizer	AE XL / *Ombra** Compressor	LC Plus†/ PARI-BOY† SX Compressor
DR_{min} (mg/min)	4.14 ± 0.18	4.17 ± 0.34
$FDF_{<5.4\mu m}$ (%)	72.1 ± 1.9	63.7 ± 2.0
$FDM_{<5.4\mu m/min}$ (mg/min)	2.99 ± 0.13	2.66 ± 0.22
TM (mg)	140.9 ± 6.2	83.4 ± 6.9

- Delivery rate data (DR_{min}) was similar for the two nebulizer / compressor systems, however $FDM_{<5.4\mu m/min}$ delivery rate was higher with the AE XL BAN/compressor than with the BEN/compressor, as a result of the higher FDF of the former
- *TM* delivered to sputter was appreciably higher for the AE XL BAN/compressor group
  - 140.9 mg compared to 83.4 mg for the BEN/compressor group

CONCLUSIONS

- The delivery rates of tobramycin using the BAN or BEN with their respective compressor systems were similar with evidence of a slightly higher fine particle delivery rate for the BAN
- The more significant difference related to the total mass delivered is somewhat expected given the higher delivery efficiency with the BAN. This higher delivery is well within the tobramycin dosage range that has been assessed clinically[1]
- The potential to adjust total delivery from the BAN, if required, exists through the adjustment of either delivery time or fill volume, or alternatively it would be possible to deliver additional dose in the same treatment session if it is considered clinically desirable to maximize delivered dose

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[1] Conway, S.P., Arch Dis Child 1999; 80:307.