



Factors Affecting Nebulized Albuterol Aerosol Particles

Nathan Itoga, MD; Christopher Kinoshita, MS; Stephen Masutani, PhD; Loren Yamamoto, MD, MPH, MBA, FAAP, FACEP
 Department of Pediatrics, University of Hawai'i John A. Burns School of Medicine and Kapi'olani Medical Center for Women & Children, Honolulu, HI
 University of Hawaii, Hawaii Natural Energy Institute



Background

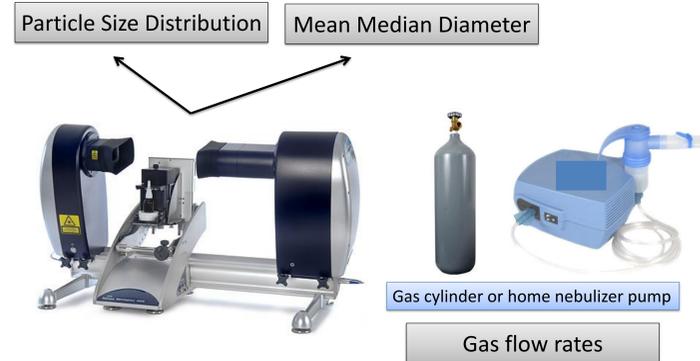
Albuterol and other asthma medications are commonly delivered to the lungs via nebulization. Particle sizes from the nebulization process should ideally be in the range of 1 to 5 microns. Particles > 5 μm tend to deposit in the upper respiratory system, whereas particles < 1 μm will remain suspended in air and do not reach the terminal bronchi. We studied several factors that affect the particle size distribution of nebulized albuterol.

Methods

Albuterol vials were nebulized under different conditions to see if any of these conditions would affect the particle size distribution.

- **Gas flow rates** - 3, 4, 5, 6, 7, 8L/minute via an adjustable flow regulated gas cylinder or via commercial home nebulizer pump with a single fixed gas flow rate
- **Fluid depth/volume within the nebulizer chamber** - 3 mL versus 6 mL
- **Age of the nebulizer** - new versus after 0, 50, 150, and 100 nebulizations
- **Nebulizer type** - semi-permanent nebulizer versus disposable single use nebulizer

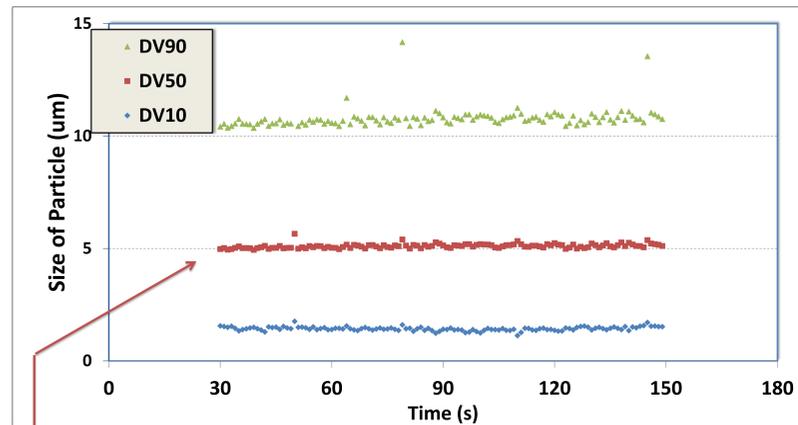
Nebulized particles were analyzed utilizing a sophisticated laser diffraction system (Malvern Instruments, Spraytec, Worcestershire, UK). This machine measures the size distribution of the nebulized particles passing through the laser detector field at 1 second intervals. Gas flow rates were recorded simultaneously with particle size measurements.



Data was collected from the instrument's software and data analysis was conducted using Microsoft Excel. Data was collected in triplicate runs,

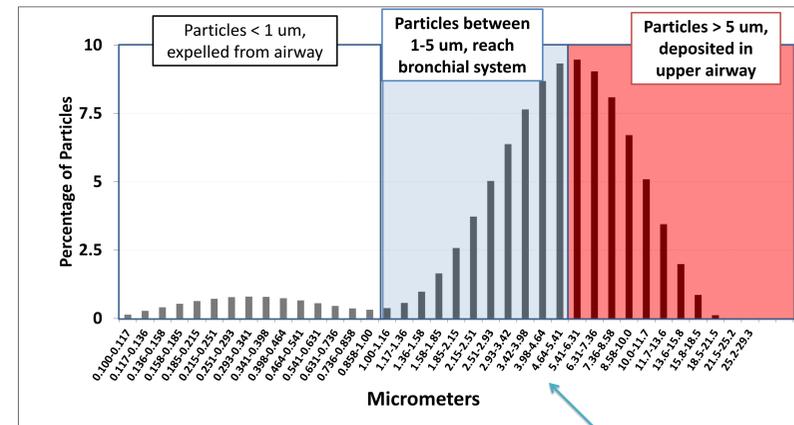
Results

Distribution of Particles Over a Single Run at 10, 50 90% - Disposable Nebulizer Albuterol (5 LPM)



Mean median diameter:
 average of median particle size of a given run

Particle Distribution Capture at 1 second Disposable Nebulizer Albuterol (5 LPM)



Percentage of Absorbable Particles:
 Particles that fall within 1.000-5.412 μm



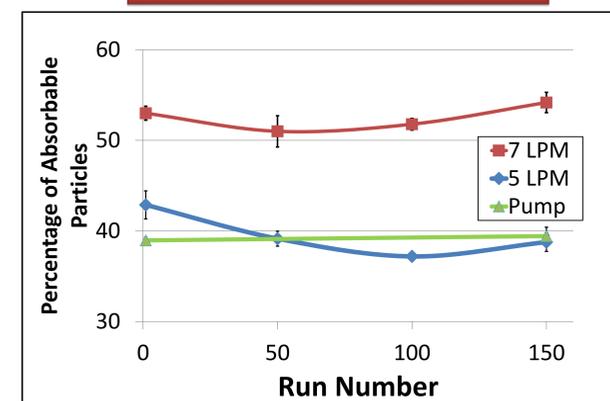
Disposable Nebulizer



Semi-permanent nebulizer

Flow Rates (Liters/minute)	Mean Median Diameter (μm)	Percentage of Absorbable Particles	Flow Rates (Liters/minute)	Mean Median Diameter (μm)	Percentage of Absorbable Particles
3	8.12 ± 0.26	16.08 ± 1.13	3	4.47 ± 0.07	56.91 ± 1.20
4	6.59 ± 0.23	27.97 ± 2.64	4	4.32 ± 0.02	57.31 ± 1.23
5	5.48 ± 0.10	40.08 ± 1.83	Pump (4.22)	4.41 ± 0.02	56.1 ± 0.51
Pump (5.2)	5.53 ± 0.02	38.96 ± 0.35	5	3.99 ± 0.02	60.05 ± 0.61
6	4.80 ± 0.16	49.51 ± 3.43	6	3.51 ± 0.04	64.24 ± 0.52
7	4.33 ± 0.19	56.42 ± 2.61			
8	4.03 ± 0.16	61.63 ± 2.65			

Aged Disposable Nebulizer



Volume Comparisons

Flow Rates (Liters/minute)	6 ml albuterol		3 ml albuterol + 3 ml ipratropium	
	MMDA (μm)	Percentage of Absorbable Particles	MMDA (μm)	Percentage of Absorbable Particles
Disposable- 8				
First 2 min	3.67 ± 0.03	66.53 ± 0.37	3.67 ± 0.08	66.96 ± 1.71
Last 2 min	3.63 ± 0.14	64.03 ± 2.55	3.74 ± 0.17	62.15 ± 0.53
Pari - 5				
First 2 min	3.59 ± 0.04	67.03 ± 1.15	3.65 ± 0.07	66.88 ± 0.57
Last 2 min	3.57 ± 0.02	66.46 ± 0.43	3.58 ± 0.08	66.01 ± 1.19

Discussion

Previous studies have shown that the gas flow rates affect the mean median diameter (MMDA), with higher flow rates leading to smaller nebulized particle sizes. This study is novel as the MMDA of nebulized particles are simultaneously measured with the percentage of particles in the 1- 5 μm range thereby quantifying the amount of particles that will be deposited in the lower respiratory system.

This study attempted to determine which factors of nebulizer systems affect the MMDA and the percentage of absorbable particles. We found that gas flow rates affect particle size to a greater degree in the disposable nebulizer compared to the semi-permanent nebulizer. We found that a flow rate of 8 liters per minute (LPM) in the disposable nebulizer is close to the particle distribution in the 5 LPM semi-permanent nebulizer system (the gas flow rate near a home pump system). Aging of a disposable nebulizer does not significantly degrade its performance. The volume of drug and type of drug may affect particle size variations to a greater degree in disposable nebulizer systems compared to semi-permanent nebulizers.

Conclusions

- This study shows that the disposable nebulizers are more sensitive to changes in gas flow rates compared to a semi-permanent nebulizer. It is therefore important to have flow rates > 8 LPM to increase therapeutic drug delivery.
- While it is simple to adjust gas flow rates in the hospital setting, home pump systems that are improperly matched with disposable nebulizers may not be adequate to supply flow rates strong enough to produce a high percentage of nebulized particles in 1-5 μm range, and may be a cause of failed home therapy
- Further work can be done using in vivo models of particle sizing that may provide better analysis of true therapeutic effects.
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