



PARI Respiratory Equipment, Inc.
White Paper

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**Comparison Testing of Competitive Portable Jet Nebulizer
Systems with Two Inhaled Medications Shows a Wide Variability
in Performance**

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Contents

Executive Summary	2
Test Results	3
Conclusions	5
Addendum	6
References	7

Executive Summary

Clinicians who prescribe inhaled medications to treat respiratory conditions such as asthma, cystic fibrosis (CF) and chronic obstructive pulmonary disease (COPD) may not have the most up-to-date information on the portable nebulizer systems that are available today. As a result, these professionals may be of the opinion that all commercially available nebulizers are equally efficient in delivering specific drug formulations and, therefore, nebulizers are interchangeable.

On the contrary, results from a recent independent study show significant variability in delivery performance of four commercially available portable nebulizer systems. Each system demonstrated unique performance characteristics during in-vitro testing with two drug formulations, underscoring their respective efficiencies and inefficiencies.

Portable nebulizer systems enable patients to take their medication on the go for a more convenient treatment and may improve adherence to therapy. However, suboptimal performance of a delivery system may lead to a poor treatment response, and may have a negative impact on patient adherence. Such situations can lead to a lack of confidence in nebulizer therapy among clinicians and patients.

The four battery-operated, portable jet nebulizer systems that were tested for delivery efficiency included:

- PARI Trek S with LC Sprint Reusable Nebulizer-

- DeVilbiss Traveler with 800 Series Reusable Nebulizer
- Respironics Mini Elite with Sidestream Plus Nebulizer
- Respironics Micro Elite with Micro Plus™ Reusable Nebulizer

All four systems were characterized with two medications, a budesonide inhalation suspension and an albuterol solution. Analyses were made of the test data to determine 1) the respirable drug delivery rate (RDDR) in micrograms per minute (ug/min) and 2) the total respirable dose delivered (RDD) measured in micrograms (ug).

RDDR is the amount of drug that is available per time unit within the respirable range. RDDR is an indicator of “how much and how fast” a drug is available for lung deposition. The respirable range being defined as drug particles from 1 to < 5 microns (um) in size. Drug particles of this size have a high probability to deposit in the lower airways of the lungs. Respirable dose delivered (RDD) is the total dose of drug available for inhalation within the same respirable range of 1 to <5um.

It may be noted that many studies evaluate nebulizer system performance by measuring particle size expressed as mass median diameter (MMD)* or mass median aerodynamic diameter (MMAD) * and respirable fraction (RF %)*. However, these

standard measures do not account for medication waste that can affect therapeutic efficacy, the respirable dose of medication available for inhalation, or the nebulization time, which may influence patient adherence.

** Please refer to the Glossary of Terms in the Addendum section below*

RDDR takes into account the respirable dose, drug delivery rate (DDR), including nebulization time, and medication waste. RDDR provides a more comprehensive assessment of delivery efficiency and is a more objective way of comparing different nebulizer/compressor systems. According to Hess ⁽²⁾, the important characteristics of nebulizer performance are the respirable dose (RD) and nebulization time. A nebulizer that delivers an effective dose in a short time period is desirable.

It follows that when prescribing portable nebulizer systems, clinicians should not only consider performance characteristics such as MMAD and RF%, but also include RDD and RDDR as part of a more meaningful evaluation of nebulizer performance.

Test Results

For budesonide delivery, it was determined that the PARI Trek S with LC Sprint Reusable Nebulizer ranked highest for overall performance for RD and RDDR. The respirable drug delivery rate (RDDR) for the Trek S was six times higher than the DeVilbiss Traveler with 800 Series Reusable Nebulizer, and delivered nearly four times the respirable dose (RDD). Compared to the MiniElite with Sidestream Plus™

Nebulizer system, the RDDR for the Trek S was three times faster and the RDD was more than forty percent higher (Figures 1 & 2).

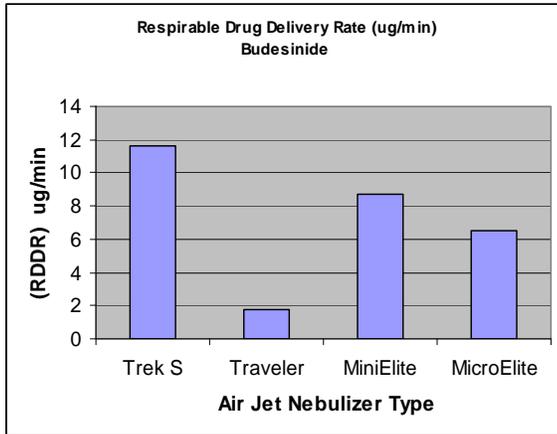


Figure 1. For budesonide – Measured values of respirable drug delivery rate (RDDR, ug/min) which is the amount of drug delivered within the respirable range per minute (the respirable range being 1 to <5 micrometers (um) and the total respirable dose delivered (RDD, ug) within the respirable range

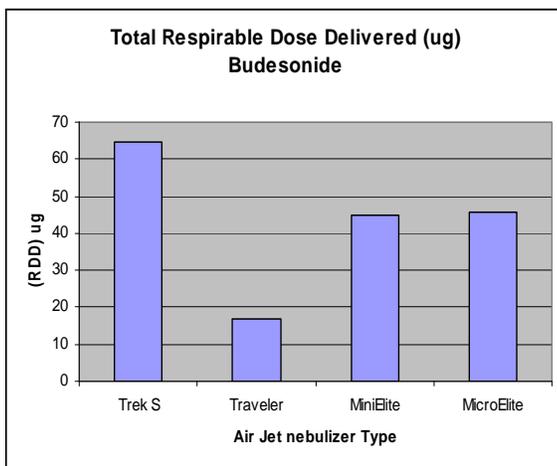


Figure 2. For budesonide – Measured values of the total respirable dose delivered (RDD ug) within the respirable range (the respirable range being 1 to <5 micrometers (um)

For albuterol it was determined that the PARI Trek S with LC Sprint Reusable Nebulizer was again the highest overall performer for RD and RDDR. Compared to the DeVilbiss Traveler with an 800 Series Reusable Nebulizer, the respirable dose of albuterol was four times higher and was delivered seven times faster. When compared with the MicroElite with a Micro Plus™ Reusable Nebulizer, the PARI TREK S with LC Sprint Reusable Nebulizer delivered more than two and one half times the respirable drug (RDD) in half the time (Figures 3 & 4).

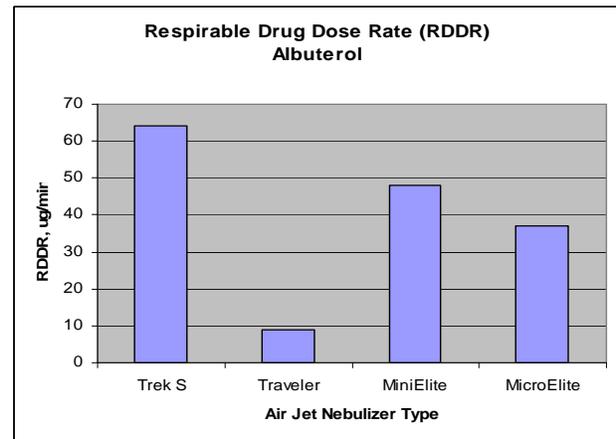


Figure 3. For albuterol – Measured values of respiratory drug delivery rate (RDDR, ug/min) which is the amount of drug delivered within the respirable range per minute (the respirable range being 1 to <5 micrometers (um) and the total respirable dose delivered (RDD, ug) within the respirable range

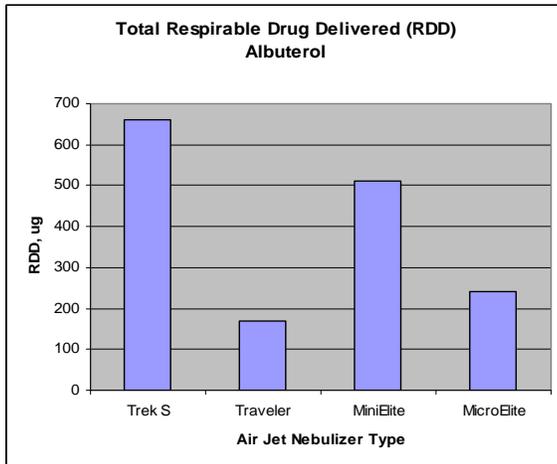


Figure 4. For albuterol – Measured values of the total respirable dose delivered (RDD, ug) within the respirable range (the respirable range being 1 to <5 micrometers (um)).

Conclusions

In the optimal setting, a clinician would be able to prescribe the desired drug and any of the available jet nebulizer systems to effectively manage and achieve control of their patient’s respiratory symptoms. However, the above test results show that wide disparities exist when the RDD and the RDDR of four competitive portable jet nebulizers are compared using a corticosteroid (budesonide) and a bronchodilator (albuterol) separately. Such variations may directly affect the therapeutic response of the patient and may very well influence the patient’s adherence to the prescribed medication.

The increasing number of available inhaler devices and device types from which to choose and prescribe for an individual patient can be very

confusing and frustrating for clinicians. However, many factors can influence the success of aerosol therapy. These include the dose uniformity that is strongly influenced by the respirable dose delivered (RDD), the cognitive and physical ability of the patient, ease of use, costs, patient preferences and system portability, which, may help encourage adherence to daily nebulizer therapy, especially in active patient populations.

In choosing a drug/device combination for a patient, it is important for the clinician to have a basic understanding of aerosol principles including how the interaction of the nebulizer- drug formulation and patient interface determines the overall efficiency of aerosol therapy. Further, understanding RDD and RDDR will provide the clinician with more meaningful information to objectively compare nebulizer delivery systems, facilitate proper device selection, and teach patients the appropriate use of aerosol devices to obtain the best possible results with aerosol therapy.

Addendum – Glossary of Terms

MMAD (or MMD) - Mass Median Aerodynamic Diameter or Mass Median Diameter Mass is used to describe a polydisperse aerosol such as that produced by most aerosol-generating devices used in clinical practice. MMAD or MMD is the particle size above and below which 50% of the mass of the particles is contained. The higher the MMAD/MMD, the more particles are of larger diameters ⁽²⁾.

Respirable Range- Aerosol particles of 1 to less than 5 microns, which reach the lung periphery. With particle sizes greater than 3 microns aerosol deposition shifts from the lung periphery to the conducting airways. Oropharyngeal deposition increases as particle size increases above 6 microns. Exhaled loss is high with particles less than 1 micron ⁽²⁾.

RF %. – Respirable Fraction
The fraction of aerosol particles in the respirable range (1 micron- <5 microns) often expressed as a percent. Example, $RF\%_{0.1-5\mu g} = 75\%$ would indicate that 75% of the aerosol particles produced were in the range of 1-5 microns.

DD – Delivered Dose...
Typically an in-vitro measurement representing the amount of drug available to the patient at the mouthpiece. Typically the measurement that FDA requires for 510K approval.

DDR – Drug Delivery Rate

DDR is a more objective and reliable parameter than nebulization time to determine and compare the speed of drug delivery. The rate of drug delivery and duration of dosing can effect patient compliance with prescribed therapy.

RDD (or RD) - Respirable Dose Delivered...

Respiratory dose delivered (RDD; mg) is the total drug delivered in the respirable range and is calculated as a product of delivery rate (mg/min), nebulization time (min) and respiratory fraction.

$$\text{Where: } RD = DD \times RF\%$$

RDDR - Respirable Drug Delivery Rate
Respirable drug delivery rate (RDDR; mg/min) is the amount of drug delivered in the respirable range per minute and is calculated as a product of the charge dose (mg/mL), delivery rate (mL/min) and respiratory fraction (%). RDDR is a predictor of intrapulmonary drug delivery over a specific time unit for a specific drug formulation and nebulizer/compressor system. RDDR is an indicator of “how much and how fast” a drug is available for lung deposition.

$$\text{Where: } RDDR = DDR \times RF\%$$

References

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