

## The Advantages of Nebulization in the Treatment of Mechanically Ventilated Neonates

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A major goal in the care of premature babies is growth, and so all therapies are applied with energy conservation in mind. While on mechanical ventilation, anything that increases the patient's work of breathing in turn increases the cost of breathing, which increases oxygen consumption, and therefore decreases the calories available for growth. Aerosolized medications that are ordered during this time add a new level of difficulty. Choosing between metered dose inhalers (MDI) and nebulizers is usually based on the preference of the respiratory therapist or physician, as the current literature is indecisive at best.

There are significant pros and cons associated with each method of delivery. For example, one problem associated with nebulizers that is well known but poorly documented is the added flow to the ventilator circuit. This increased flow causes increases in ventilator pressures and volumes, can impede or prevent triggering of the ventilator for spontaneous breaths, and can cause triggering difficulties with flow or pressure-triggered breaths. In these cases, the ventilator no longer acknowledges the patient's efforts to breathe, basically leaving the patient on continuous positive airway pressure (CPAP) between timed breaths. These unsupported breaths can cause an increased work of breathing, leading to increased caloric expenditure and decreased weight gain. This will also make weaning from the ventilator more difficult, as the patient's respiratory muscles are already taxed.

A 1989 study by Beaty et al. highlighted problems with pressure support ventilation (PSV) and triggering during nebulization in adults. The study detailed two cases in which patients in PSV were unable to initiate breaths during nebulization with small-volume nebulizers (SVN) that were powered with an external air

source.<sup>1</sup> Other options are available, such as ventilators with integrated nebulization ability. These are designed to subtract flow from the circuit to power the nebulizer, ending up with the same total flow. Another option, ultrasonic nebulizers, do not add additional circuit flow but have many problems that have limited their clinical utility, such as excessive heat and weight, which requires placement at the ventilator. Metered dose inhalers may obviate the need for SVN devices in some, but not all, situations; however, not all necessary medications are available in MDI form. In addition, depending on the FIO<sub>2</sub> and propellant gas volume, a hypoxic gas mixture may be given in children with V<sub>T</sub> of 100ml or less; however, dead-space and compressible volume also must be considered.<sup>2</sup> Yet another option, dry powder inhalers, are not appropriate for use during mechanical ventilation.

When using SVNs to deliver aerosolized medications inline, clinicians are usually left manually decreasing ventilator settings so that the outcome after the added flow is equal to the ordered settings. This may be effective in controlling pressure and volume increases, but also lends itself to problems, such as the possibility of forgetting to return to original settings, which can be detrimental to the patient. Most importantly, this solution does not solve the resultant inability to trigger ventilator breaths. In the fragile neonatal population these problems are amplified.

In 2002, another option entered the market: the Aeroneb® Professional Nebulizer System (Aeroneb Pro), (Aerogen, Inc., Mountain View, CA), a novel nebulizer that claims to add no extra flow during nebulization. This new nebulizer technology is currently available for many uses, including medication delivery during mechanical ventilation, and utilizes a unique micropump aerosol generator (called "OnQ™") to create respirable particles without additional flow.<sup>3</sup> One of the purported benefits of the Aeroneb Pro is that it contributes no

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external flow into the ventilator circuit, thereby relieving the known hazards.

To ascertain whether this claim was accurate and to compare the Aeroneb Pro to existing nebulizers, in June 2003 my research partner and I set up a model of a mechanically ventilated, spontaneously breathing neonate. A Servo 300 ventilator (S300) (Siemens, Danvers, MA) was used to ventilate a double bellows test lung (Michigan Instruments, Grand Rapids, MI) driven by an LTV-1000 (Pulmonetics, Minneapolis, MN) to simulate an infant spontaneously breathing at 40 B/min.

Three different nebulizers were used for comparison: a Misty-Neb™ conventional small volume nebulizer (SVN) (Allegiance, McGaw Park, IL), a MiniHeart® SVN (Westmed Inc, Tucson, AZ), and the Aeroneb® Pro (Aerogen, Inc., Mountain View, CA). Airway resistance was created using a 2.5mm ID endotracheal tube (ETT) (Mallinckrodt, Pleasanton, CA) and lung compliance was set at 1 ml/cm H<sub>2</sub>O. The SVN devices were tested with the S300 in the pressure control/SIMV mode. Ventilator settings were the same for all test conditions: frequency (f): 30 B/min, inspiratory time (T<sub>I</sub>): 0.4 seconds, PEEP: 4 cm H<sub>2</sub>O, peak inspiratory pressure (PIP): 15 cm H<sub>2</sub>O above PEEP, pressure support level (PSV): 10 cm H<sub>2</sub>O above PEEP, and sensitivity set to the most sensitive flow trigger setting without auto-triggering. The LTV was adjusted to insure that each spontaneous effort was sensed by the S300 during control conditions (C) resulting in a PSV supported inspiration. An unaltered infant circuit was used for the control.

Three test conditions were evaluated: the Aeroneb Pro was operated electronically according to the manufacturer's recommendations (#1), 6 L/min of flow was used to power the Misty-Neb (#2), and 2 L/min powered the MiniHeart (#3). All three nebulizers were placed in the inspiratory limb of the control circuit at the temperature probe adapter. V<sub>T</sub>, f, minute volume (MV), PIP, PEEP, and T<sub>I</sub> measurements were made using a CO<sub>2</sub>SMO differential pressure transducer (Novamatrix, Wallingford, CT) placed between the ventilator circuit and the ETT for independently displayed values (IDV) for the control and all test conditions.

The results highlighted the aforementioned problems associated with conventional nebulizers during mechanical ventilation.

#### Volume change:

- Condition #2 resulted in an increased total MV and a decrease in volume delivered for spontaneous efforts. The total MV increased because, even though there was less support for spontaneous efforts, the mechanical breaths were increased.
- Condition #3 caused a decrease in total MV, possibly because of dyssynchrony, and a decrease in support of spontaneous efforts.
- Condition #1 shows no evidence of change compared to the control.

#### Pressure change:

- #2 caused an increase in PIP of 13.10 cm H<sub>2</sub>O from control and an increase in set PEEP.
- #3 also caused an increase in PIP and PEEP to a lesser extent than condition #2.
- #1 shows no evidence of change compared to the control.

#### Patient-ventilator dyssynchrony:

- #2 caused a decrease in acknowledged spontaneous effort (V<sub>T</sub>S) and an increase in T<sub>I</sub> due to added flow.
- #3 resulted in a decrease in total MV, due to unrecognized spontaneous efforts during added flow.
- #1 again caused no change in settings compared to the control.

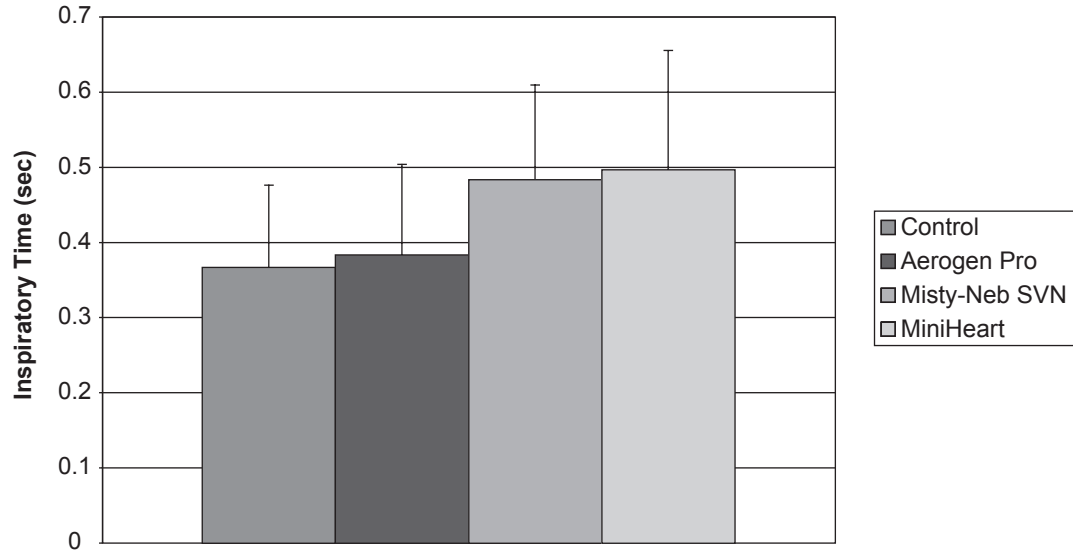
Compared to the control, condition #1 resulted in the least alteration in set ventilation parameters and patient-ventilator synchrony. Decreased V<sub>T</sub>S and increased T<sub>I</sub> during conditions #2 and #3 reflect patient-ventilator dyssynchrony not evident during condition #1.

- Condition #1 causes the least change in delivered volumes, inspiratory time, and pressures relative to the control.
- Condition #2 results in the most overall change in chosen parameters.

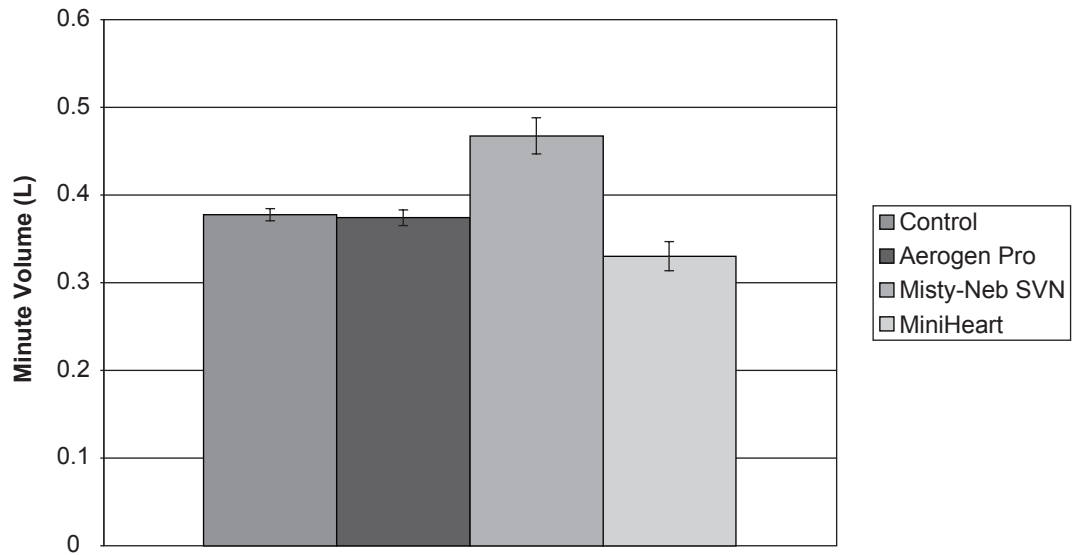
**Figure 1**

	<b>MV total (L)</b>	<b>V<sub>T</sub> S (ml)</b>	<b>T<sub>I</sub> (sec.)</b>	<b>PIP (cm H<sub>2</sub>O)</b>	<b>PEEP (cm H<sub>2</sub>O)</b>
<b>Control (SD)</b>	0.38 (0.01)	6.10 (0.00)	0.37 (0.11)	18.67 ( 2.32)	4.51 (0.04)
<b>#1 Aeroneb Pro (SD)</b>	0.37 (0.01)	6.11 (0.03)	0.38 (0.12)	18.70 ( 2.32)	4.47 (0.05)
<b>#2 Misty-Neb (SD)</b>	0.47 (0.02)	1.49 (0.08)	0.48 (0.13)	31.77 (10.34)	5.90 (0.07)
<b>#3 MiniHeart (SD)</b>	0.33 (0.02)	1.62 (0.04)	0.50 (0.16)	19.31 ( 5.81)	4.86 (0.05)

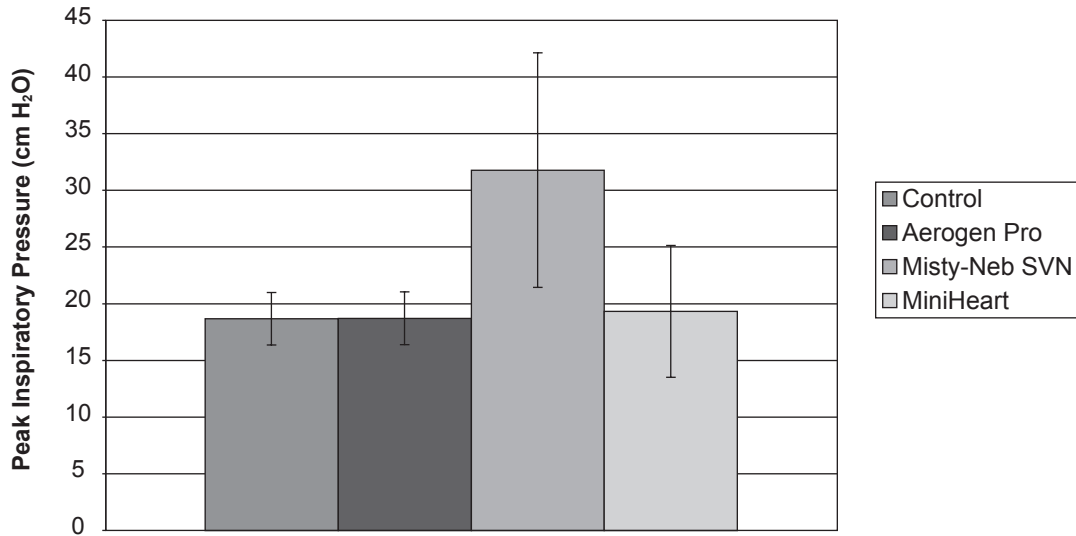
### Inspiratory Time Comparison Among Four Techniques for Aerosol Delivery



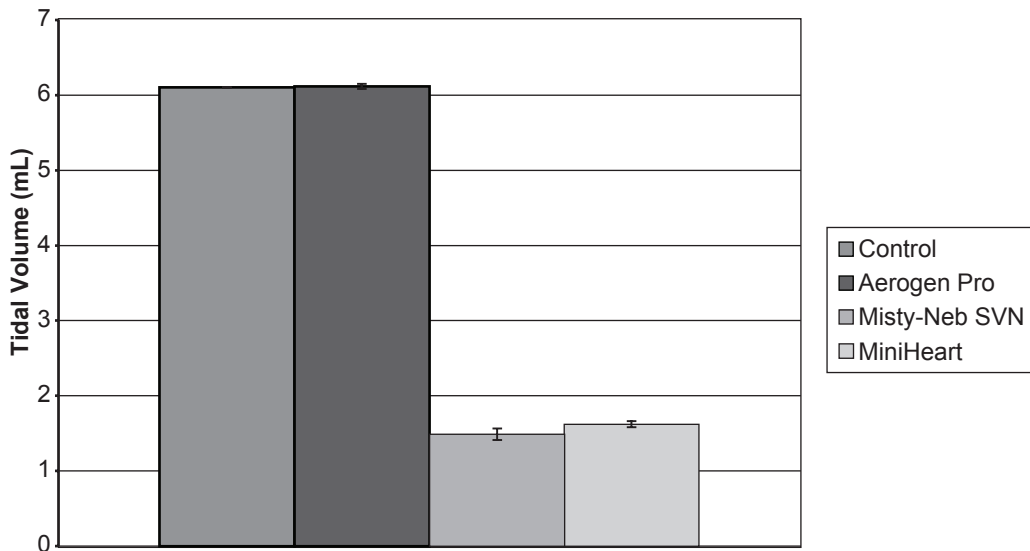
### Minute Volume Comparison



### Comparison of Four Nebulizers Effect on Peak Inspiratory Pressure during Mechanical Ventilation



### Spontaneous Tidal Volume



Clinically, the Misty-Neb caused over-distention, relative hyperventilation, and patient-ventilator dyssynchrony. Over-distention, as evidenced by a 41% increase in PIP and a 24% increase in set PEEP, can lead to barotrauma. An increase in minute volume from 0.38 L to 0.47 L caused a calculated drop in arterial pCO<sub>2</sub> from 40 mmHg to 32 mmHg, leading to hyperventilation. Patient-ventilator dyssynchrony can be seen as a drastic (76%) decrease in V<sub>T</sub>S and a 35% increase in T<sub>I</sub>. The MiniHeart caused dyssynchrony and relative hypoventilation. Dyssynchrony is most evident in the decrease in MV and V<sub>T</sub>S and the increase in T<sub>I</sub>. A decrease in MV from 0.38 to 0.33 calculates an increase in arterial pCO<sub>2</sub> from 40 mmHg to 46.1 mmHg leading to relative hypoventilation. There is no evidence of these problems with the Aeronob Pro.

Lung over-distention and patient-ventilator dyssynchrony are a problem in any patient population; however, the consequences may be more obvious and detrimental in neonates and infants. Weight gain is a major focus of medical care for these patients, and so it is vital to control work of breathing (WOB) to decrease energy expenditure in order to facilitate growth. An increased WOB can also delay weaning from the ventilator due to respiratory muscle fatigue.

The Aeronob Pro, condition #1, alleviates the problems associated with flow added by either a conventional or MiniHeart SVN in this test model. Clinical correlation with this bench model is indicated.

This study was created in order to (1) prove or disprove the claim that the Aeroneb Pro adds no flow to the ventilator circuit and (2) compare it to previously used nebulizers. Our data has convinced me that there is indeed no flow added into the ventilator circuit during use of the Aeroneb Pro. All set and monitored parameters were unchanged from the control, unlike the conventional nebulizers. The ventilator recognized every simulated spontaneous breath, also unlike the conventional nebulizers. The comparison to these other nebulizers is not only striking, but highlights a potentially dangerous common practice. The Aeroneb Pro, by allowing the ventilator to maintain the chosen settings and trigger sensitivity, reduces the risk of harm to neonates receiving aerosolized medications. When caring for such a fragile patient population safety is of utmost importance. The Aeroneb Pro provides this safety over conventional nebulizers.

## REFERENCES:

- 1 "Continuous In-line Nebulizers Complicate Pressure Support Ventilation" Beaty, Ritz, and Benson: Chest 1989; 96:1360-63
- 2 "Aerosol Therapy for Children" Rubin and Fink: Respiratory Care Clinics of North America 2001; Vol. 7 No.2: 202
- 3 Aerogen Technology Review and Performance Report for the Aeroneb® Professional Nebulizer System, 2002 ■