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EDITORIAL

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Maximizing aerosol delivery during mechanical ventilation: go with the flow and go slow

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During the past decade the unprecedented improvements in technology for delivery of inhaled drugs were matched by an equally impressive growth in clinical applications. Especially notable were the impressive gains in knowledge and understanding of methods to deliver inhaled therapies to mechanically ventilated patients. In the recent past optimal techniques for delivery of inhaled drugs to patients receiving mechanical ventilation were defined, and they are now widely applied in clinical practice. Early on investigators employed γ-scintigraphy after administration of radiolabeled aerosols to determine lung deposition in ventilator-dependent patients [1, 2]. These investigators suggested that the efficiency of aerosol delivery is significantly lower in mechanically ventilated than in ambulatory patients. Thus in the early 1990s the consensus of opinion was that the ventilator tubing and endotracheal tube are formidable barriers to effective drug delivery in ventilator-supported patients. The reduced efficiency of drug delivery meant that much larger doses of drugs than those employed in ambulatory patients were needed in mechanically ventilated patients. Recently several investigators reported that when the technique of administration is carefully employed, aerosol delivery in mechanically ventilated patients is comparable to that in ambulatory, nonintubated patients [3, 4]. In fact, with some of the newer generation of aerosol devices that are designed specifically for use in ventilator circuits aerosol delivery in ventilator-supported patients may surpass that in ambulatory patients [5].

In vitro tests are invaluable in determining the contribution of each of a host of factors that influence aerosol delivery during mechanical ventilation [3]. With bench models that simulate the conditions in a ventilator-supported patient the effects of ventilator settings and circuit conditions, aerosol generating device configuration, and drug formulation on drug delivered to the lower respiratory tract are by now well known. The results of in vitro investigations contribute significantly to the development of logical recommendations for use of nebulizers and metered dose inhalers (MDIs) in ventilator-dependent patients [3, 4]. Careful application of these techniques maximizes clinical responses in mechanically ventilated patients.

The major drawback of in vitro tests is that measurement of drug *delivery* is relatively straightforward, but the *amount of drug deposited* and its *site of deposition* in the lung cannot be determined with these techniques. The ventilator tubing and endotracheal tube serve as an extended baffle that filters out higher velocity, larger drug particles within the aerosol. The finer, well-entrained drug particles are trapped on filters placed at the distal end of the ventilator tubing or endotracheal tube. The amount of drug deposited on the filter is representative of lower respiratory tract delivery; the implicit assumption is that these finer particles (mostly 1–2 μm in size) within the aerosol should deposit diffusely within the lung. However, the amount of exhaled drug cannot be determined by in vitro tests alone. This drawback can be partially overcome by using a "mass balance" technique that matches ventilator circuits and ventilatory parameters to determine the correlation between the results of in vitro tests and those in patients receiving mechanical ventilation [6]. Despite the drawbacks mentioned above, carefully performed in vitro tests are important for guiding aerosol therapy during mechanical ventilation.

In their contribution to *Intensive Care Medicine* Hess and colleagues [7] compared aerosol delivery during pressure-controlled (PCV) to that during volume-controlled ventilation (VCV). Although PCV is a commonly employed mode of ventilation in the intensive care unit, there was no information about the efficiency of aerosol delivery from jet nebulizers and pressurized MDIs with this mode of ventilation. Aerosol delivery is likely to differ between PCV and VCV because the pattern of inspiratory flow, i.e., the inspiratory waveform, differs in the two modes of ventilation. Moreover, the lung mechanics affect the inspiratory flow pattern and the duration for which inspiratory flow is provided during PCV. Hess and coworkers [7] employed a bench model to compare albuterol delivery with two inspiratory flow patterns during VCV (constant flow or descending ramp flow) to that obtained during PCV. The authors also varied the lung mechanics by selecting two settings of resistance and compliance to represent high or low time constants. For each condition they measured the amount of aerosol delivered with inspiratory times of 1 or 2 s. Efficiency of the jet nebulizer to deliver aerosol was influenced by the inspiratory time, pattern of inspiratory flow, and lung mechanics. In contrast, the efficiency of drug delivery from a MDI was not influenced by any of the factors mentioned above and was remarkably steady under the various conditions of the study. The consistency and reliability of dose delivery, regardless of the inspiratory flow pattern and lung mechanics, favor the use of MDIs over jet nebulizers for aerosol delivery during mechanical ventilation. Notably, efficiency of the jet nebulizer during PCV was significantly lower than during VCV (p=0.03). Significant variations in drug delivery could influence optimal patient management when a jet nebulizer is employed to administer bronchodilators to patients with acute exacerbations of asthma or chronic obstructive pulmonary disease who are receiving mechanical ventilation with PCV.

Slower inspiratory flows increase aerosol delivery to the lower respiratory tract in ambulatory [8] and in ventilator-dependent patients [3, 9, 10]. Previous investigators have also observed a direct correlation between aerosol delivery with a higher duty cycle (inspiratory time (T_I)/duration of total breathing cycle (T_{TOT}) [9, 10, 11]. With a jet nebulizer Hess and coworkers [7] also found greater albuterol delivery with a longer inspiratory time. In contrast to the findings of Fink and colleagues [9, 10], the present study did not report a greater amount of aerosol delivery with a higher duty cycle when a MDI was employed. Although longer inspiratory times (higher T_I/T_{TOT}) improve aerosol delivery, routine clinical use of longer inspiratory times may be complicated by worsening dynamic hyperinflation if the expiratory time is unduly shortened. For routine clinical use slower inspiratory flow rates should be preferred over longer inspiratory times to maximize aerosol delivery [10]. In addition, it is crucial for aerosol generation to be synchronized with inspiratory flow from the ventilator. When an aerosol is employed for drug therapy in a ventilator-dependent patient, it is best to "Go with the flow and go slow."

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References

1. MacIntyre NR, Silver RM, Miller CW, Schuler F, Coleman ER (1985) Aerosol delivery in intubated, mechanically ventilated patients. Crit Care Med 13:81–84
2. Fuller HD, Dolovich MB, Posmituck G, Wong Pack W, Newhouse MT (1990) Pressurized aerosol versus jet aerosol delivery to mechanically ventilated patients: comparison of dose to the lungs. Am Rev Respir Dis 141:440–444
3. Dhand R, Tobin MJ (1997) Inhaled bronchodilator therapy in mechanically ventilated patients. Am J Respir Crit Care Med 156:3–10
4. Duarte AG, Fink JB, Dhand R (2001) Inhalation therapy during mechanical ventilation. Respir Care Clin N Am 7:233–260
5. Dhand R (2002) Nebulizers that use a vibrating mesh or plate with multiple apertures to generate aerosol. Respir Care 47:1406–1416
6. O'Riordan TG, Palmer LB, Smaldone GC (1994) Aerosol deposition in mechanically ventilated patients: optimizing nebulizer delivery. Am Rev Respir Dis 149:214–219
7. Hess DR, Dillman C, Kacmarek RM (2003) In vitro evaluation of aerosol bronchodilator delivery during mechanical ventilation: pressure-control versus volume control ventilation. Intensive Care Med (http://dx.doi.org/10.1007/s00134-003-1792-1)
8. Dolovich MA (2000) Influence of inspiratory flow rate, particle size, and airway caliber on aerosolized drug delivery to the lung. Respir Care 45:597–608
9. Fink JB, Dhand R, Duarte AG, Jenne JW, Tobin MJ (1996) Deposition of aerosol from metered-dose inhaler during mechanical ventilation: an in vitro model. Am J Respir Crit Care Med 154:382–387
10. Fink, JB, Dhand R, Grychowski J, Fahey PJ, Tobin MJ (1999) Reconciling in vitro and in vivo measurements of aerosol delivery from a metered-dose inhaler during mechanical ventilation and defining efficiency-enhancing factors. Am J Respir Crit Care Med 159:63–68
11. O'Riordan TG, Greco MJ, Perry RJ, Smaldone GC (1992) Nebulizer function during mechanical ventilation. Am Rev Respir Dis 145:1117–1122