Aerosol Bronchodilator Therapy During Noninvasive Positive-Pressure Ventilation: A Peek Through the Looking Glass

Exacerbations of chronic obstructive pulmonary disease (COPD) are a common cause of acute respiratory failure,[1] leading to over 700,000 hospitalizations annually in the United States.[2] Approximately 50% of patients suffering hypercapnic respiratory failure from exacerbations of COPD require some form of ventilatory support.[3] The ventilatory strategy employed in such patients has evolved during the past decade, and noninvasive positive-pressure ventilation (NPPV) is now considered as a first-line modality of mechanical ventilation for patients with exacerbations of COPD resulting in hypercapnic respiratory failure.[4–6] In NPPV, alveolar ventilation is augmented by application of positive pressure through a nasal or oral mask, thereby avoiding the need for an endotracheal or tracheostomy tube.

Patients receiving NPPV also require inhaled bronchodilators for relief of airway obstruction. Unfortunately, there is a paucity of information regarding use of aerosol therapy in patients receiving NPPV,[7–11] a situation analogous to the one that existed for use of inhaled bronchodilators with invasive mechanical ventilation in the 1980s. Over the past 2 decades, the factors influencing inhaled bronchodilator therapy during invasive mechanical ventilation have been elucidated, and guidelines have been developed to optimize clinical practice.[12] For NPPV, development of guidelines needs greater understanding of the factors influencing aerosol drug delivery during this mode of ventilation. Therefore, the paper by Branconnier and Hess in this issue of the Journal[13] is especially timely.

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These investigators employed a bench model to study the factors influencing drug delivery with a metered-dose inhaler (MDI) and a nebulizer during NPPV. With a bilevel-positive-airway-pressure ventilator (Respironics S/T 30) set at an inspiratory pressure of 15 cm H_2O and an expiratory pressure of 5 cm H_2O, they found that the position of the leak port (whether in the circuit or incorporated in the face mask) influenced nebulizer efficiency.[13] On the other hand, synchronization of MDI actuation with inhalation was important for MDI efficiency.[13] These findings provide a glimpse into the extraordinary complexity of delivering aerosols during NPPV.

Variations in the type of aerosol generator employed (MDI or nebulizer), the position of the aerosol generator, type of ventilator, inspiratory flow rate, ventilator settings, position of the leak port, circuit conditions, the density of the inhaled gas, type of mask employed, mask size, amount of leak, and patient characteristics are just some of the factors that could affect inhaled drug delivery during NPPV. High inspiratory flow rates employed during NPPV increase turbulent flow and produce higher inertial forces, causing greater impaction of particles in more central airways.[14,15] On the other hand, application of positive pressure increases tidal volume and reduces the respiratory rate, which are both factors that tend to enhance aerosol delivery.[16] Moreover, increase in expiratory time could allow more time for sedimentation of drug particles and could alter the pattern of drug deposition during exhalation.[16]

The efficiency of aerosol delivery with positive-pressure ventilation cannot be assumed, as was demonstrated by Dolovich and colleagues[17] for intermittent positive-pressure breathing, which was at one time the most popular method for delivering aerosol therapy. Initial enthusiasm for administration of bronchodilators with this technique was dampened by the observation that it decreased the efficiency of drug delivery, compared to spontaneous breathing.[17]

Several investigators have determined drug delivery with nebulizers during NPPV. In a bench model, continuous positive airway pressure set at a level of 10 cm H_2O reduced drug delivery from a jet nebulizer.[8] Furthermore, there was a 5-fold variation (between 5% and 25% of the nominal dose) in the amount of albuterol delivered by a jet nebulizer, depending on the placement of the nebulizer in the circuit, the inspiratory and expiratory positive pressure settings, and the breathing frequency employed.[11] Fauroux and coworkers[10] assessed the effectiveness of aerosol delivery with NPPV in children with stable cystic fibrosis. The deposition of a radiolabeled aerosol from a nebulizer synchronized to deliver aerosol during inspiration was about 30% greater with pressure-support ventilation, compared to use of the nebulizer alone.[10]

Preliminary clinical studies with nebulizers have been performed during NPPV,[8] but patients with stable asthma or COPD were enrolled in most of them. For example, Parkes and Bersten[8] employed a crossover design in 9 stable asthmatics, and found a significant bronchodilator response to nebulized albuterol with both conventional nebulization and nebulization during continuous positive airway pressure. Only one group of investigators have determined the efficacy of aerosolized bronchodilators in acutely ill patients (ie, under conditions of actual NPPV). In an emergency department, Pollack and co-investigators[7] randomized patients suffering from acute asthma to receive aerosolized albuterol delivered via either nebulizer alone or via bi-level positive airway pressure with nasal or oronasal mask. Patients receiving bi-level positive airway pressure had a significantly greater increase in peak flow than patients who received nebulizer therapy without application of positive pressure.

Only one group of investigators has determined the efficiency of drug delivery with an MDI during NPPV. Nava and colleagues[9] investigated the clinical response to equivalent doses of albuterol delivered via MDI during NPPV, during spontaneous breathing using an MDI with spacer, and during intermittent positive-pressure breathing in stable patients with COPD. These investigators found that bronchodilator delivery via MDI with spacer during NPPV is feasible and produces a significant bronchodilator effect.[9]

Thus, most clinical studies indicate that aerosolized bronchodilator therapy is effective during NPPV. However, the efficiency of aerosol delivery under a variety of conditions in patients receiving NPPV for acute respiratory failure remains poorly understood. The findings of Branconnier and Hess[13] should focus our attention on the need to optimize settings for inhaled drug delivery in the setting of NPPV, so that patients may derive the maximum benefits from bronchodilator therapy.

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