Nebulized Drug Delivery in Patients Breathing Spontaneously Through an Artificial Airway

During the past 25 years, incremental gains in knowledge about aerosol delivery to mechanically ventilated patients had a major impact on patient care in this setting. The complex array of factors influencing aerosol delivery during mechanical ventilation made it difficult to elucidate the contribution of individual parameters to optimal aerosol delivery. Over the ensuing years, bench models made invaluable contributions in elucidating the effects of each variable on the efficiency of aerosol delivery and in determining methods to maximize drug deposition in the lung, despite the poor efficiency of aerosol-generating devices, the presence of a ventilator circuit and artificial airway, differing ventilator modes and ventilatory parameters, and in many clinical situations, the occurrence of severe lung disease in the patient.[1]

The artificial airway was long believed to be a serious obstacle to effective aerosol delivery during mechanical ventilation. Impaction of aerosol on the endotracheal tube reduced the efficiency of lower airway delivery of drug, particularly in pediatric ventilator circuits (internal diameter of the artificial airway between 3 mm and 6 mm).[2,3] However, nebulizer efficiency was not reduced with endotracheal tubes of internal diameter $\geq$ 7 mm.[4] Earlier investigators may have overemphasized the impediments created by the artificial airway to aerosol delivery, probably because the aerosol generator was placed too close to the artificial airway. When the aerosol generator was placed at a distance from the endotracheal tube, instead of being directly connected to it, drug losses in the endotracheal tube were minimized and pulmonary deposition of aerosol was increased.[4] Overall, in mechanically ventilated adults, the type of aerosol generator and the ventilatory parameters seemed to have a greater influence on aerosol deposition within the endotracheal tube than the diameter of the endotracheal tube per se.[4]

Critically ill patients in the ICU often require placement of an artificial airway to provide mechanical ventilation. In some situations (eg, during recovery from anesthesia or during weaning trials), patients may have an endotracheal tube while they are breathing spontaneously. Spontaneously breathing patients may also have tracheostomy tubes for extended periods while they are being weaned from the ventilator. Moreover, spontaneously breathing patients with chronic respiratory failure may require a tracheostomy tube, but no or periodic ventilator support, for a prolonged duration. Many such patients require aerosolized therapies, particularly inhaled bronchodilators, for relief of air-flow obstruction. In spontaneously breathing patients the efficiency of aerosol delivery is influenced by the drug output from the nebulizer, aerosol particle size, interface between the nebulizer and patient, and breathing pattern.[5] Addition of an artificial airway in a spontaneously breathing patient adds another variable influencing aerosol deposition to the mix. Optimal methods for delivering aerosols in the setting of patients needing an artificial airway without ventilator support have not been well studied.

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In this issue of the Journal, Ari and colleagues employed a bench model of spontaneous respiration to study the efficiency of aerosol delivery across artificial airways.[6] These investigators employed an anatomical teaching manikin with both bronchi attached to a collecting filter, using a Y adapter. The manikin was intubated with either an endotracheal tube (8.0 mm internal diameter) or a tracheostomy tube of similar internal diameter. The model was attached to a sinusoidal pump that simulated the breathing pattern of a spontaneously breathing adult. The tracheostomy tube was tested with a tracheostomy collar, T-piece, or manual resuscitation bag, whereas only a T-piece and manual resuscitation bag were employed for testing with the endotracheal tube. After each nebulizer treatment the drug deposited on the filter was expressed as a percentage of the nominal dose placed in the nebulizer. Comparison of various interfaces showed that a T-piece provided twice as much aerosol as a tracheostomy collar. Likewise, Piccuito and Hess also found higher efficiency of aerosol delivery when a nebulizer was connected to a T-piece instead of a tracheostomy mask.[7]

Ari and co-workers observed that use of a manual resuscitation bag with either an endotracheal or tracheostomy tube was associated with a 3-fold increase of aerosol delivery, compared to the other interfaces.[6] The investigators matched the number and timing of the breaths delivered with the manual resuscitation bag to an independently run breathing simulator. The higher aerosol delivery could be explained by the fact that the end of the tubing was capped when the manual resuscitation bag was employed, whereas when the other interfaces were employed, the tubing was open to the atmosphere and the breaths were generated by the spontaneous breathing simulator connected to the artificial airway. The relatively closed system model used in experiments with the manual resuscitation bag allowed the circuit to be charged with the drug. Higher drug deposition on the filter could be explained by the effects of nebulizer flow carrying the drug onto the filter. Because the nebulizer operated continuously, drug deposition on the filter could occur both during inspiration and expiration in a closed system, and this would lead to a higher value for drug deposition on the filter. In contrast, when a T-piece or tracheostomy collar was employed, most drug deposition on the filter would occur only during inspiration, and drug deposition on the filter would be proportionately lower.

Aerosol delivery through tracheostomy tubes has not been evaluated with the same degree of detail as with endotracheal tubes. Tracheostomy tubes are generally shorter and more curved than endotracheal tubes, and some of them have inner cannulae that reduce the inner diameter of the tube and could influence drug delivery. All of these variables determine the proportion of aerosol that deposits on the tube en route to the lung. Ari and colleagues found that a greater percentage of the nebulized dose was delivered with the tracheostomy tube than via the endotracheal tube.[6] Previously, O'Riordan and colleagues determined that aerosol deposition in the tracheostomy tube was only 2.6% of the nebulizer output during inspiration and that there was not much difference with different tracheostomy tube sizes (between 6 and 10 mm).[8] However, these investigators[8] employed a specialty nebulizer that produces an aerosol with a finer particle size, compared to standard jet nebulizers, such as the one employed by Ari and co-workers.[6]

In spontaneously breathing patients, Ari and co-workers found that aerosol delivery with tracheostomy tubes was higher than with endotracheal tubes, and a T-piece connected to a nebulizer provided higher aerosol deposition than a tracheostomy collar.[6] If even higher levels of aerosol deposition are required, such as in patients experiencing severe bronchoconstriction, a manual resuscitation bag connected to a T-piece could be connected to a tracheostomy tube. Capping one end of the T-piece could allow rapid delivery of higher drug amounts with a manual resuscitation bag. When drugs are administered by the manual resuscitation bag technique, patients would need appropriate monitoring for adverse side effects caused by rapid systemic absorption of larger amounts of drug delivered to the lung.

It is sobering to realize how little was known about aerosol delivery in the ICU setting only 25 years ago. The science of delivering aerosols in critically ill patients has made great strides since then, and carefully performed studies with models that simulate the clinical scenario have helped to improve techniques for aerosolized drug delivery. Bench models of mechanical ventilation played an important role in elucidating the optimal techniques of aerosol delivery and made a substantial impact on patient care in the ICU. The work of Ari and co-workers[6] clarifies the effect of various interfaces on nebulizer efficiency and provides new information for treatment of a subset of intubated, spontaneously breathing patients.

Muhammad Mir MD
Rajiv Dhand MD FAARC
Department of Medicine
University of Tennessee Graduate
School of Medicine
Knoxville, Tennessee

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Correspondence: Rajiv Dhand MD, Department of Medicine, University of Tennessee Graduate School of Medicine, 1924 Alcoa Highway, U114, Knoxville TN 37922. E mail: rdhand@mc.utmck.edu.

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