Effective aerosol therapy in children

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Running head: Aerosol therapy
Aerosol therapy is a mainstay for the treatment of airway diseases. Medication delivered by aerosols is generally less expensive, works more rapidly, and produces fewer side effects in the same medications delivered systemically. As well medications can often be delivered to the airways that would otherwise be rendered ineffective if given systemically.

The requirements for aerosol therapy depend greatly on the target site of action and the underlying disease. Asthma medications should deposit on the conducting airways while peptides intended for systemic absorption would require deposition at the alveolar capillary bed. Examples of the latter include insulin for the treatment of diabetes and inhaled growth hormone (1). Effective deposition requires ultrafine particles to allow them to penetrate to the deep lung, a slow inhalation, and relatively normal airways that do not hinder aerosol penetration. Furthermore the forces needed to generate the aerosol should not degrade these proteins.

Classically, aerosol bronchodilators and inhaled corticosteroids (ICS) are used to treat asthma. Effective deposition requires particle size and inspiratory flow appropriate for airway deposition with sufficient resident time in the airway to allow sedimentation. Generally this means high efficiency production of particles between 0.5-5 µm mass median aerodynamic diameter (MMAD) inhaled with a slow inspiratory flow and a breath hold. Many devices have been developed to facilitate effective inhalation. Some common reasons for therapeutic failure of these aerosol medications include the use of inactive or depleted medications, inappropriate use of the aerosol device, and poor adherence to prescribed therapy (2, 3).

There are additional challenges when aerosol medications are used in infants and small children (4), or during an acute asthma attack. Rapid respiratory rate and patient anxiety lead to depositing more drug in the oral pharynx and less in the airways. Airway obstruction and inhomogeneous ventilation may also limit the targeted deposition of medications. Although all of the commonly used aerosol devices (jet nebulizers, pressurized metered dose inhalers, and dry powder inhalers) have been shown to be equally effective when used correctly the ability to use these during an acute asthma exacerbation may be compromised.
These challenges are even greater when the patient is in respiratory failure on a mechanical ventilator. Depending on humidification within the ventilator circuit and the ventilator duty cycle there may not be adequate time for the aerosol cloud to develop in the circuit and the geometry of the circuit may hinder the deposition of the aerosols in the airway (5).

Other medications that have been used for the treatment of airway disease include mucolytics such as dornase alfa used to treat cystic fibrosis (CF) and aerosolized antibiotics such as tobramycin solution. Pulmonary deposition of these medications can be severely compromised when the airway is filled with pus. Both dornase and aerosol antibiotics are unlikely to penetrate to the deep lung despite good devices (6). It is possible that the use of surfactants as a carrier or as a therapeutic agent may help to clear the airways and to transport medication such as these into the deeper lung.

This challenge is even greater when delivering gene therapy vectors to the airway. These are very large molecules often unstable to nebulization, requiring precise dosing, and administered to patients with lung disease. Nevertheless techniques are being developed to improve the deposition of these vectors in the lungs particularly of patients with CF (7).

The nasal passage is an additional target for drug therapy. Pump inhalers have been used to administer decongestions or corticosteroids to the nose but deposition into the sinuses is poor. Because of the importance of sinus deposition of antibiotics and other medications for the treatment of chronic sinusitis there is active investigation not only into developing devices for nasal inhalation but also mechanisms (such as humming after inhalation) that may help to deposit medications within the nose and sinuses (8).

Despite the mechanical and engineering challenges in designing devices for aerosol administration, the clinician's greatest challenge is patient education to use their medications and aerosol devices appropriately (3).
References


3. Rubin BK. What does it mean when a patient says, "My asthma medication is not working?" Chest. 2004;126:972-81.


