EDITORIAL

Inhalation Delivery of Drugs

What would be a more natural goal for the treatment of pulmonary diseases than by the administration of aerosolized drugs directly to the lungs? This approach would minimize systemic side effects, especially if the drug is rapidly metabolized or taken up by binding sites on the lung surface, thereby improving drug efficacy at reduced cost to the patient. Inhalation therapy is critically dependent on the ability to consistently deliver metered doses of drugs to the patient's lungs. Treatment efficacy is closely related to the maximal lung deposition of the drug (*1*). This, in turn, requires a reliable nebulizer and consistent techniques of aerosol delivery. Such aerosol treatments are currently used to deposit a variety of drugs in the lungs, including pentamidine for patients with pneumocystis carinii pneumonia (*1*), gentamicin for patients with cystic fibrosis (*2*), and steroids and bronchodilators for patients with asthma (*3*). Treatment of patients with adult and neonatal respiratory distress syndrome with aerosolized synthetic surfactant also shows promise (*4*).

The interesting article by Virgolini et al. (*5*) in this issue of the *Journal of Nuclear Medicine* brings into focus the rapid development of new immunomodulating, antibacterial, and antiviral drugs requiring direct localized delivery to the lungs for future therapeutic intervention. Nuclear medicine should be poised to expand its horizons beyond the diagnostic base to take advantage of further improvements in aerosol generation and delivery. We also should use our recognized capabilities for testing in vivo the new ^{123}I- and ^{99m}Tc-labeled drugs being developed. These in vivo studies will be designed to provide the basis for effective clinical dosing of patients with pulmonary diseases undergoing inhalation therapy by determining the new drugs' pulmonary deposition patterns, whole-body distribution and safety. This approach would also provide a fruitful area of interaction between nuclear medicine and pulmonary medicine, which would lead beyond the most common nuclear medicine application, namely the evaluation of patients suspected of having pulmonary embolism.

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Virgolini et al. (*5*) showed that ^{123}I-labeled recombinant interferon gamma 1b (IFNg), administered as an aerosol, can be safely used to determine its pulmonary deposition pattern, whole-body distribution and safety in normal volunteers. They also achieved localized activation of mononuclear phagocytes in the lungs. Serious systemic side effects and an immune response (*6*) seen in systemically administered IFNg were minimized. However, good drug delivery to the lungs of normal subjects does not necessarily guarantee similar results in the lungs of patients. Their study must, therefore, still be extended to clinical studies with patients who may have airway obstruction and other flow limitations. Treatment with IFNg is a good example of the need to deliver a drug directly to the lungs. Recent studies (*7*) had confirmed its clinical efficacy in the treatment of patients with a variety of pulmonary diseases by augmenting the role of alveolar macrophages in pulmonary host defense. Preclinical research with rodents (*8*) had established that IFNg transfer in the lungs, however, is almost completely unidirectional from the bronchoalveolar space to the plasma pool, suggesting that direct pulmonary deposition is required for the most effective treatment of IFNg responsive pulmonary diseases.

Improved devices for aerosol administration are now available that allow a more precise deposition of aerosol in the lungs, enhancing the prospects for successful inhalation therapy (*9*). The factors influencing this procedure are very complex and include: (a) the drug's properties, especially its solubility and hygroscopy, which must facilitate its inhalation; (b) the nebulizer system which must produce particles <3 μm in size for maximal lung deposition; and (c) the inhalation maneuver, which affects the amount and deposition pattern of the inhaled aerosol. The amount of medication that deposits in the patient's lungs is expressed as percentage of the drug placed in the nebulizer actually inhaled, and proportion of the inhaled drug either deposited or exhaled from the lungs (*10*).

Previous aerosol studies have suggested that nebulizers are very inefficient in delivering aerosolized medication to the lungs of patients supported by mechanical ventilation. However O'Riordan et al. (*10*) were able to demonstrate that, by optimizing nebulizer and ventilator factors, mechanically-ventilated patients inhaled ~31% of the nebulizer charge with a relatively high (~15%) pulmonary deposition of nebulized medication. These results are similar to those obtained by nonintubated, spontaneously breathing individuals. They found that nebulizer type, ventilator setting, nebulizer fill volume, treatment time and humidification are the principal factors that affect aerosol delivery.

Our future progress as a specialty will depend, in part, on our ability to adapt to the rapidly changing developments in molecular biology and the resultant improvements in drug therapies. Since many of these new drugs will be cytokines and similar compounds, which are rapidly metabolized when administered systemically, the ability to deliver them directly to the lungs is crucial for efficaceous therapy. Fortunately, this process is being greatly facilitated by the improved techniques of nebulization and aerosol delivery which are now becoming available.

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