Effect of Ethanol on Droplet Size, Efficiency of Delivery, and Clearance Characteristics of Technetium-99m DTPA Aerosol

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With recent technical advances in aerosol technology, the study of regional ventilation using [^{99m}Tc]DTPA aerosol has become increasingly popular. Using a cascade impactor, we have assessed droplet size distribution from a newly designed nebulizer. Delivery efficiency of [^{99m}Tc]DTPA aerosol to normal subjects was improved 70% with a 10% concentration of ethanol in the nebulizer. Using filter paper fixed to the delivery end of the aerosol device, and varying ethanol concentrations from 0–10%, an 87% increase of deposited radioactivity is measured. Use of higher concentration of ethanol to the nebulizer solution did not further improve delivery efficiency. The addition of ethanol did not alter clearance characteristics of [^{99m}Tc]DTPA from the lung nor did it affect droplet size distribution.

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Because the distribution of aerosol droplets in the lungs during inspiration is dependent on particle size (*1–5*), we thought it desirable to measure the average size of droplets produced with a newly acquired aerosol system.* Our initial studies showed that this system was capable of delivering sufficient radioactivity in 5 min to achieve a count rate of 100,000 counts per min. Although this count rate was adequate for planar gamma camera imaging, it was considered to be about a factor of 2 below that needed to obtain suitable tomographic images. Thus, we have also sought ways to improve the efficiency of delivery of aerosols generated by this system in order to avoid increasing the breathing time beyond 5 min. To this end the effect of decreasing surface tension by adding ethanol to the solution prior to ventilation was assessed. As a logical extension of this latter study, we have measured clearance half-times of radioactivity from the lungs to ascertain what effect, if any, ethanol might have. Such an effect, if present, could have an important bearing on clearance studies in various pulmonary disorders caused by scleroderma, pneumoconiosis, sarcoidosis, acute smoke inhalation, or radiation therapy (*6–14*).

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MATERIALS AND METHODS

Measure of particle size

A seven-stage cascade impactor† was used to measure particle size (*15*). A krypton-85 charge neutralizer‡ was inserted into the system between the nebulizing device and the impactor to eliminate the effects of static electricity (*16*). For this portion of the experiment, the oxygen flow rate through the nebulizer was set at 9 l/min. A Sierra instrument series # 100 constant flow vacuum pump provided the necessary suction (Fig. 1). A concentration of ethanol in the technetium-99m diethylenetriaminepentaacetic acid ([^{99m}Tc]DTPA) solution of 20% by volume was used.

Measurement of delivery efficiency

After appropriate consent forms were obtained, 13 normal, nonsmoking subjects aged 20–35 with no history of lung disease

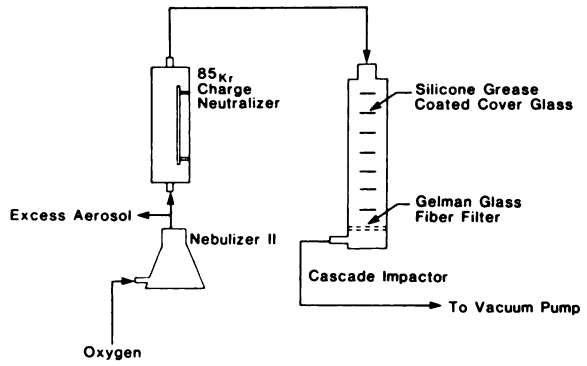

FIGURE 1
Apparatus for measurement of particle size distribution

were studied. From 30 to 50 mCi of [^{99m}Tc]DTPA was placed in the nebulizing device together with various quantities of ethanol and a sufficient volume of normal saline to bring the final volume to 2 ml for each study. After fully explaining the procedure to the subject, the device was attached while the individual continued to breathe room air while lying supine. A nose clip was then placed. The aerosol was then generated using oxygen at a flow rate of 10 l/min. The subjects continued to breathe at maximal tidal volume for varying periods of time up to 5 min. A large field-of-view gamma camera was positioned against the posterior thorax. The count rate was continuously monitored and recorded during the rebreathing maneuver. In two instances repeat studies were performed on successive days in order to compare the efficiency of delivery with no ethanol added to that obtained using concentrations of ethanol up to 20% by volume.

As an alternative method for assessing the effect of ethanol on delivery efficiency, measurements were made of the deposition of [^{99m}Tc]DTPA aerosol on Whatman No. 1 filter paper fixed to the delivery end of the aerosol device. Final concentrations of ethanol from zero up to 50% were used for this part of the study.

Effect of ethanol on effective clearance half-time

Immediately upon completion of aerosol inhalation, the assessment of clearance commenced with subject and camera placements as before. Data were acquired by way of computer for 1 min at 9, 15, 30, 60, and 90 min after cessation of aerosol inhalation.

RESULTS

Table 1 summarizes the results of four measurements of droplet size. There was no significant difference in the mass median aerodynamic diameter of the droplets obtained when the radioactive solution contained either no ethanol or 20% ethanol (0.23 and 0.22 μ, respectively). Likewise, the standard deviation of droplet size was found to be essentially the same under both experimental conditions.

TABLE 1
Effect of 20% Ethanol Concentration on Droplet Size Distribution

Item	No ethanol	Ethanol
Median diameter (μ)	0.23	0.22
Mass median aerodynamic diameter (μ)	0.25	0.24
Geometric s.d.	2.05	2.00

The graphical results obtained from the studies of two volunteers who breathed either the [^{99m}Tc]DTPA aerosol with a 10% ethanol mixture or without ethanol (control) are shown in Fig. 2. Although the tidal volumes for the two subjects are quite different, activity accumulates within the lungs in a linear fashion for both. With ethanol added, the delivery efficiency is increased ~70% over that of control levels in these two volunteers.

The data obtained from the collection of aerosol droplets on filter paper are shown in Fig. 3. An average increase of 87% of deposited radioactivity over control values is noted with a 10% concentration of ethanol in the nebulizer. The use of higher concentrations of ethanol to the solution in the nebulizer did not further enhance the delivery rate of aerosol droplets.

The results obtained from measurement of effective clearance half-times as a function of ethanol concentration in the DTPA solution are summarized in Fig. 4. There was no significant change in the effective clearance half-times of radioactivity using ethanol concentrations from zero to 40%. Average $T^1/_2$ effective was 56.0 ± 11.1 min.

DISCUSSION

Based on several studies on the lung deposition of aerosols, it would appear that the ideal size for aerosol

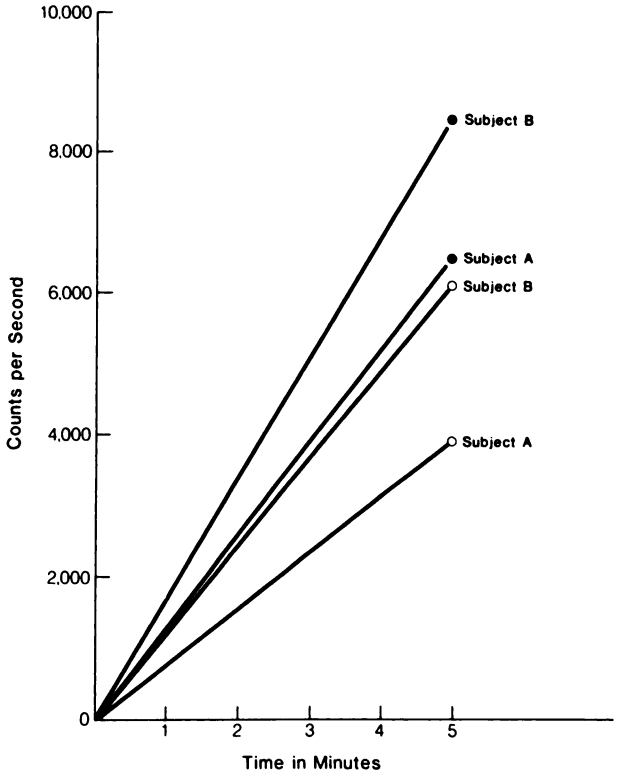

FIGURE 2
Effect of 10% ethanol concentration in [^{99m}Tc]DTPA solution in two normal subjects. (●) With ethanol; (O) Without ethanol

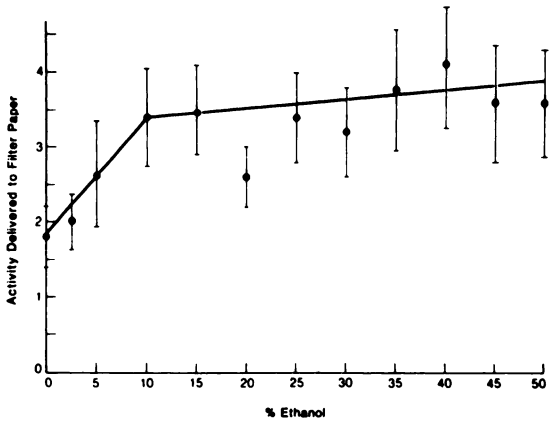

FIGURE 3
Activity delivered to filter paper. Curve is result of five replicate experiments

droplets in order to get good uniformity in the lungs during deep tidal volume breathing should be between 0.1 and 0.5 μ (*1,2*). Our study shows that the nebulizing system we are using produces a particle size of 0.23 μ which seems ideal. It is of interest that the particle size is unaltered by the addition of ethanol despite the fact that the addition of ethanol to 10% by volume produces a significant increase (almost a factor of 2) in the number of aerosol droplets produced per unit of time. We postulate that the introduction of ethanol to [^{99m}Tc]DTPA solution produces a significant decrease in surface tension, thus increasing the volatility and formation of aerosol droplets. These aerosol droplets are then carried by convection of oxygen flowing into the nebulizing system into the upper airway during tidal volume breathing.

The ability of ethanol to increase delivery efficiency of aerosol droplets was demonstrated in vitro and confirmed in two normal subjects. Our institution now routinely evaluates regional ventilation using this method. To date we have imaged over 200 patients and are currently investigating the clinical utility of [^{99m}Tc]DTPA aerosol in the evaluation of regional ventilation in cystic fibrosis (*17*).

Our measurement of clearance half-times of [^{99m}Tc]DTPA from the lungs of normal controls showed that 10% ethanol in the nebulizer has no effect on clearance rate of radioactivity from the lungs. Apparently, this concentration of ethanol does not alter the integrity of the alveolar membrane as does cigarette smoke and other noxious materials (*7–12*). Our clearance rate in normal subjects (56.0 ± 11.1 min) correlates well with normal clearance rate determined by Susskind et al. (53 ± 7 min) and Crawley et al. (59 ± 5 min) (*12, 14*).

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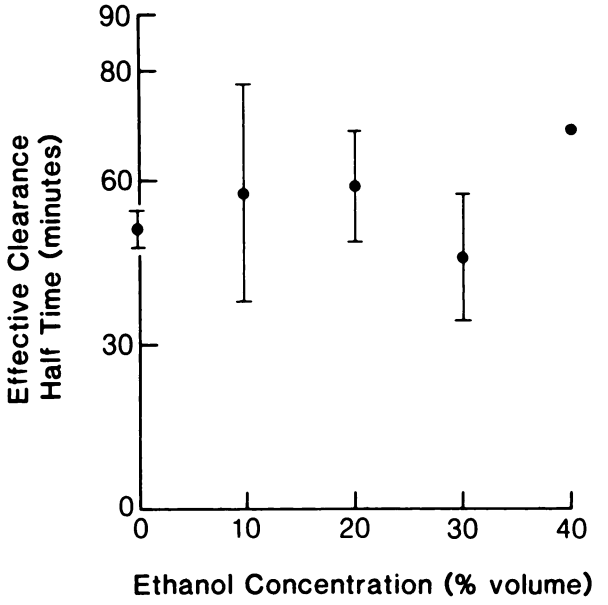

FIGURE 4
Effect of various ethanol concentration on effective clearance half-times. Data are result of one to four replicate experiments

FOOTNOTES

* UltraVent, (formerly SynteVent®, Synaco, Inc., Palo Alto, CA), Diagnostic Products Div., Mallinckrodt Inc., St. Louis, MO.

† Marple cascade impactor, Minneapolis, MN.

‡ Thermal Company, Inc., St. Paul, MN.

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