Optimizing Aerosol Lung Deposition in Cystic Fibrosis Patients

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Summary

Lung deposition measurements with inhaled radiolabelled aerosol particles where performed in 5 adult CF patients. The inhalation was controlled with an AKITA® delivery device. Aerodynamic particle size was 3.5 µm. Intrathoracic lung deposition was found to be 86 % of the emitted dose with very little intersubject variability.

Introduction

Aerosol systems used for inhalation therapy should be able to deliver drugs into different regions (e. g. bronchi, lung periphery) of the respiratory system. However, efficiency and reproducibility of particle deposition in the lung in most of the commercially available aerosol systems is limited by their delivered particle size distribution and the breathing pattern of the patients. Even if particle size is optimised (between 2 µm and 4 µm aerodynamic particle diameter, d_{ae}), the efficiency and variability of lung deposition is strongly affected by the patient's breathing pattern [1]. Patients with cystic fibrosis (CF) show chronic infections of the respiratory tract and progredient impairment of lung function even in young age. Due to the progression of their pulmonary disease, these patients have strong restrictions of life quality and lifetime. In principle, progression of pulmonary disease in these patients may be slowed down by consequent inhalation therapy. However, this treatment requires re-

producible deposition of drugs in the pulmonary regions of interest. Aim of our study was the optimisation of pulmonary particle deposition in CF patients by an optimised breathing manoeuvre.

Patients

5 CF patients participated in this study, 4 male and 1 female. The patients were on average 33 years old (69 kg and 1.78 m) with a mean FEV_1 of 69 % (% predicted; range 50 % - 95 %).

Materials and Methods

Intrathoracic lung deposition was determined with ^{99m}Tc labelled Fe_3O_4 aerosol particles (d_{ae} = 3.1 µm) produced by means of an improved air driven spinning top generator as prior described [2]. Aerosol concentration was enhanced using a virtual impactor. These particles are very stable in the lungs. The inhalation manoeuvre was performed in a standardized manner by means of an AKITA® inhalation device. The inhalation volume was individualized taking into account the patient's vital capacity (IVC) and the flow rate was fixed to 200 ml/s during in- and exhalation without endinspiratory breath hold time. After end of the inhalation procedure regional deposition was measured as prior described by means of a planar gamma camera and a human body scintillation counter. Peripheral lung deposition was determined by measuring particle retention in the lungs 24 hours after inhalation. In brief, the method allows the determination of total deposition, intrathoracic and extrathoracic deposition as well as bronchial and peripheral deposition [3].

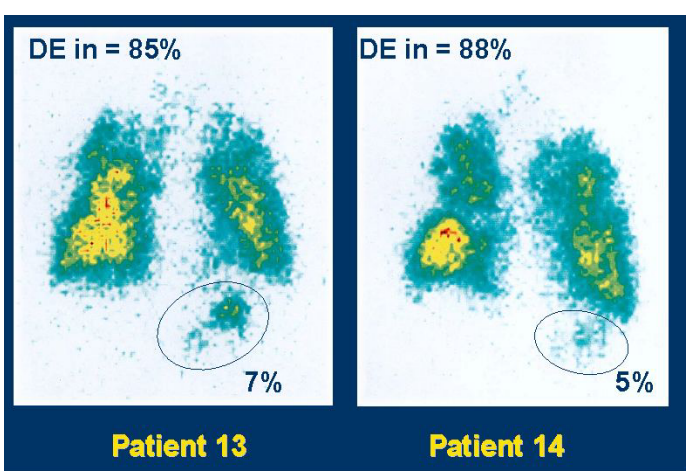

Figure 1: Gamma Szintigraphy of two CF patients after Aerosol Deposition with controlled deposition using an AKITA inhalation device

Results

Intrathoracic lung deposition in our patients was 86.3 % ± 1.4 % (mean ± SD) of the emitted aerosol. On the other hand the extrathoracic deposition was only 5.8 ± 1.8 %) (Fig. 1). It is obvious that these data stand in strong contrast to the results obtained in prior investigations of patients with chronic obstructive pulmonary disease (COPD) and CF using spontaneous breathing with conventional inhalation techniques. Only 7.9 % ± 1.1 % of the administered aerosol was found on an exhalation filter. Peripheral lung deposition, determined as intrathoracic deposition 24 hours after end of the inhalation was 77,8 ± 4,7 %. The obtained values of regional deposition showed only minor interindividual variations between the different patients (Fig. 2).

Discussion

In our study we used a standardized inhalation manoeuvre which was controlled by means of the AKITA® aerosol delivery system. The AKITA® device itself is a delivery device that individually controls the breathing pattern and can be combined with commercially available jet nebulizers. A slow and deep inhalation manoeuvre allows the inhaled particles (d_{ae} between 2 – 5 µm) to penetrate via the oropharynx and larynx into the lungs without being deposited by impaction in the upper respiratory tract. After reaching the lungs particles are deposited mainly by sedimentation. Our patients showed a pulmonary deposition of 85 % of the emitted dose, which is much more than the values obtained

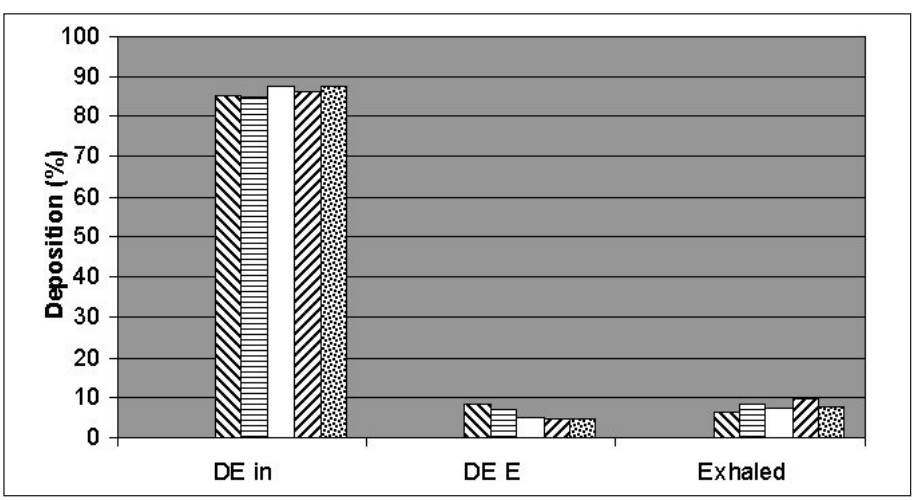

Figure 2: Intrathoracic (DE in) and extrathoracic (DE E) deposition and the exhaled fraction for the 5 individual patients

without standardization in prior studies, which usually report data between 10 and 30 % [4]. The very high pulmonary and very low extra pulmonary deposition was achieved without endinspiratory breath hold times. This suggests that endinspiratory breath hold is not necessary because of the slow and deep breathing allowing the residence time of particles in the lungs to be long enough for a sufficient deposition. In addition, the interindividual variability in lung deposition was extremely low.

Our data suggest that the AKITA® delivery system allows an efficient pulmonary deposition of aerosol particles sized between 2 µm and 5 µm using a standardized breathing manoeuvre. It seems likely that the described optimised breathing manoeuvre allows a reproducible administration of sufficient pharmacon doses (e. g. antibiotics, a_1-proteinase inhibitor) in CF patients.

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