Lung (2003) 181:149–155
DOI: 10.1007/s00408-003-1016-z

Lung

The Effects of One-Week Fluticasone Propionate Inhalation Therapy for Tc-99m DTPA Radioaerosol Distribution in Asthma of Children: A Preliminary Report

A.-C. Chen,[1] F.-J. Tsai,[1] J.J.P. Tsai,[2] C.-C. Lin,[3] C.-C. Lee,[4] and A. Kao[4]

[1]Department of Pediatrics, China Medical University Hospital, Taichung, Taiwan
[2]Graduate Institute of Bioinformatics, Taichung Healthcare and Management University, Taichung, Taiwan
[3]Department of Family Medicine, China Medical College Hospital, Taichung, Taiwan
[4]Department of Medical Research, China Medical College Hospital, No. 2, Yuh-Der Road, Taichung 404, Taiwan

Abstract. This study evaluated the effects of fluticasone propionate inhalation therapy for the distribution pattern of Tc-99m DTPA radioaerosols in 10 children with asthma. The homogeneous degree of depositing Tc-99m DTPA radioaerosol was evaluated using a modified standard score system over the bilateral lungs. The baseline scores were calculated from Tc-99m DTPA radioaerosol inhalation lung scintigraphy before inhalation therapy (100 μg fluticasone propionate two times daily for one week), and the scores were recalculated after inhalation therapy to evaluate the effects of one-week of fluticasone propionate inhalation therapy for Tc-99m DTPA radioaerosol distribution patterns. After one week of fluticasone propionate inhalation therapy, the scores were decreased in all of the 10 children, which may mean that the bronchial constriction degree due to asthma is decreased. In addition, there was a significantly statistical difference in the scores before and after one-week fluticasone propionate inhalation therapy ($p < 0.05$). In conclusion, one-week fluticasone propionate inhalation therapy could significantly improve the bronchial constriction due to asthma in children based on the evidence of Tc-99m DTPA radioaerosol inhalation lung scintigraphic findings.

Key words: Fluticasone propionate inhalation therapy—Tc-99m DTPA radioaerosol—Asthma

Correspondence to: A. Kao; email: albertkaotw@yahoo.com.tw

Introduction

Airway inflammation is considered to be the primary pathogenic mechanism underlying asthma [5]. Inflammation of the airway is present even in asthmatic patients with only mild episode asthma [14]. The more severe the asthma is the greater likelihood of permanent structural damage to the airways as a result of persistent inflammation [5]. The risk has increasingly led physicians to stress the importance of prompt treatment with inhaled anti-inflammatory therapy. Indeed, the latest revision of the British Thoracic Society Guidelines [13] recommends use of inhaled corticosteroids for any patients using an inhaled bronchodilator more than once a day. In recent studies [7, 8], fluticasone propionate inhalation therapy was shown to be effective in the treatment of asthmatic children, resulting in improved lung function and control of asthma symptoms.

There has been an increase in the use of Tc-99m DTPA radioaerosols in clinical investigations. Tc-99m DTPA radioaerosols, generated by a jet nebulizer, are inexpensive, readily available and have good scintigraphic quality. Tc-99m DTPA radioaerosols have replaced radioactive gases, such as Kr-81m and Xe-133, in many hospitals. Therefore, Tc-99m DTPA radioaerosol lung scintigraphy has been used to visualize lung ventilation (LV) in various diseases [3, 6].

The present study tried to use the Tc-99m DTPA radioaerosol lung scintigraphy to quantitatively investigate the effects of one-week fluticasone propionate inhalation therapy in asthma of children.

Materials and Methods

Patients

Ten patients (5 boys, 7 girls; age: 6–12 years old) who fulfilled the American Thoracic Society Criteria for asthma were studied [2]. They were having various treatments, but all treatments were withheld for 24 hours before the studied. The baseline study was performed before 100 μg fluticasone propionate inhalation therapy two times daily for one-week, then the study was repeated after inhalation therapy.

Tc-99m DTPA Radioaerosol Inhalation Lung Scintigraphy

Tc-99m was chelated to DTPA (Daiichi Radioisotope, Tokyo, Japan) by introducing 50 mCi of Tc-99m pertechnetate into a vial containing 20 mg DTPA and 2.2 mg tin chloride. Tc-99m DTPA was prepared no more than 1 hour before use. Tc-99m DTPA radioaerosol was generated by a commercial lung aerosol delivery unit (AERO/VENT, model AV-400 MEDI-NUCLEAR, California, USA) containing 15–30 mCi Tc-99m DTPA in 2 ml saline. The radioaerosol droplet size was measured by an inertial impactor (Model PC-2, California Measurement Inc, California, USA). The mass median aerodynamic diameter (MMAD) of the Tc-99m DTPA radioaerosol was smaller than 1 μm with an oxygen air flow rate of 7 L/min. All of the studied subjects were in the supine position and inhaled for 2 min from the aerosol delivery unit until the total radioactivity was over 200,000 counts by a normal tidal breathing. Data were collected as a 512×512 matrix with word mode size by means of a large field of view computerized gamma camera over the posterior view, including the whole lungs, and the static

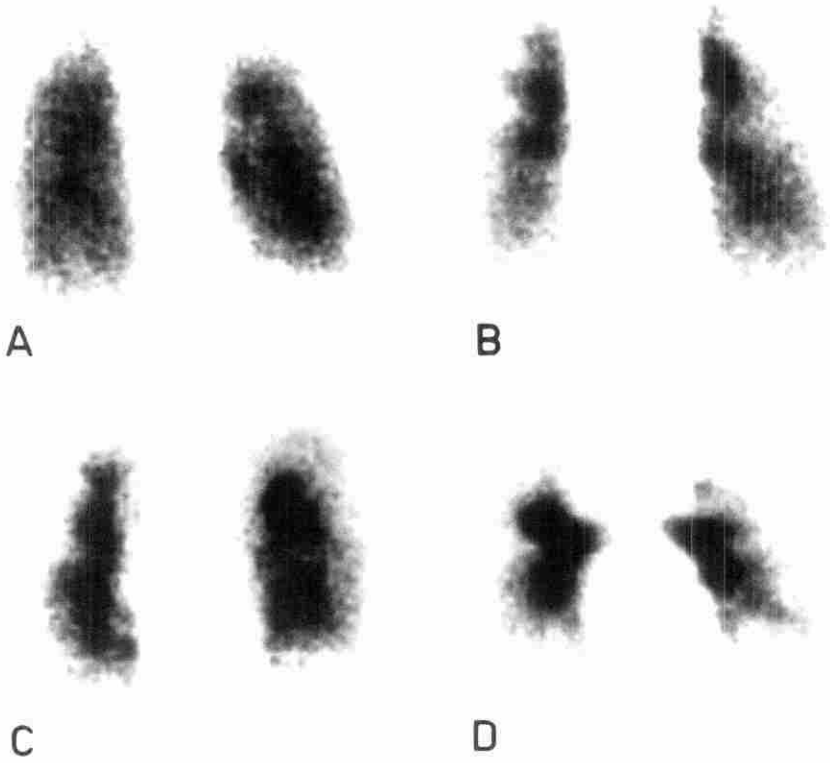

Fig. 1. The figures demonstrate the Tc-99m DTPA radioaerosol inhomogeneous distribution patterns in (**A**) normal, (**B**) mild abnormality, (**C**) moderate abnormality, and (**D**) severe abnormality.

imaging is represented as an X-ray film. Two independent observers evaluated the images and calculated the homogeneous scores according to the following criteria [3, 6]: the more bronchial obstruction is intense, the higher the homogeneity score. If the two doctors' results are different, the third doctor will review the images again. The same results of any two of the three doctors' scores are accepted. Homogeneity score-(**A**) Inhomogeneous distribution: (1) normal and homogeneous distribution is 0 point (Fig. 1A). (2) Mild abnormality is 1 point, when (a) slightly excessive deposition in the central airways or (b) slightly uneven distribution involving less than 25% of the pulmonary parenchyma, or (c) both (Fig. 1B). (3) Moderate abnormality is 2 points, when (a) definitely excessive central deposition or (b) distinctly uneven deposition in the smaller airways involving 25–50% of the lung (Fig. 1C). (4) Severe abnormality is 3 points, when gross abnormalities of deposition in either the central or peripheral airways, together with absent or reduced deposition in more than half of the pulmonary parenchyma (Fig. 1D). (**B**) Base to apex gradient: (1) The score is 0 point, if the radioactivity is balanced. (2) The score is 1 point if the radioactivity distribution is inverted (Fig. 2). **(C)** Segmental defects: (1) The score is 0 point, if the activity distribution defect is smaller than one segment. (2) The score is 1 point, if the activity distribution defect is larger than or equal to one segment (Fig. 3).

Results

Detailed data of the homogeneity scores including inhomogeneous distribution, base to apex gradient, and segmental defects in asthma patients are shown in

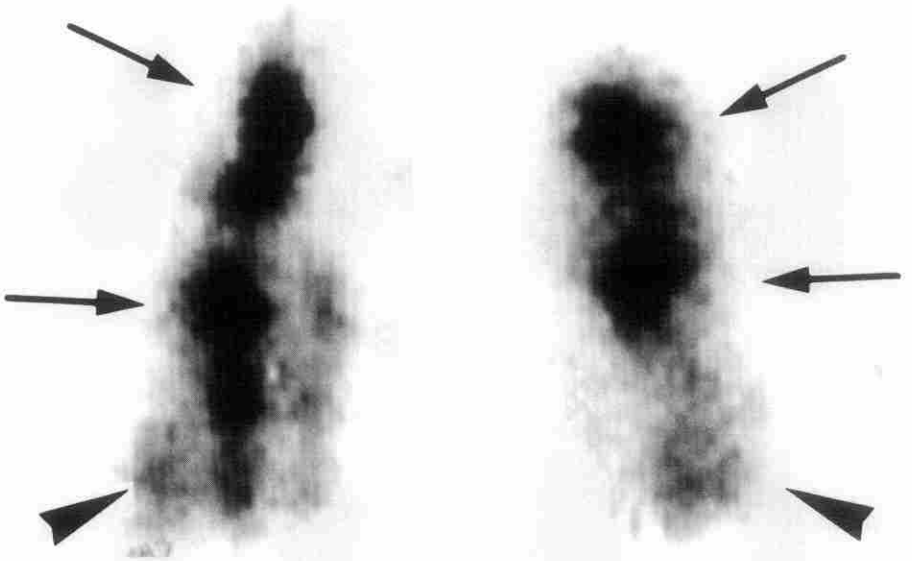

Fig. 2. The imaging demonstrates a typical pattern of an inverted base to apex gradient in the Tc-99m DTPA radioaerosol lung scintigraphy. The increased tracer accumulation in the upper portions (arrows) and decreased tracer accumulation in the lower portions (arrowheads) of bilateral lungs are noted.

Table 1. After inhalation therapy, the scores are decreased in all of the 10 children (Table 1). Before and after inhalation therapy, there were statistically significant differences in the total homogeneity scores including inhomogeneous distribution, base to apex gradient, and segmental defect (p values <0.05 by Wilcoxon signed-rank tests).

Discussion

Inflammation of the airway mucosa plays an important role in the pathogenesis of airway asthma [9, 10]. Inflammation may induce airway narrowing because of an increase in the volume of tissue or the luminal contents produced by an inflammatory exudation or secretion in the airway [15]. Early intervention with anti-inflammatory medications such as inhaled corticosteroids may delay progression of asthma and maximize lung function [1]. Therefore, the narrowing airway could result in a poor distribution of inhaled Tc-99m DTPA radioaerosols into the peripheral lung. However, early antiinflammatory treatment of patients with asthma using corticosteroids is expected to increase the distribution of inhaled Tc-99m DTPA radioaerosols into the peripheral lung. Therefore, the study tried to use the quantitative Tc-99m DTPA radioaerosol lung scintigraphy to investigate the change in the homogeneity score of the radioaerosols in children with bronchial asthma.

Tc-99m DTPA radioaerosol inhalation lung scintigraphy has been used in clinical practices for nearly 30 years [11, 12]. In this study, Tc-99m DTPA radi-

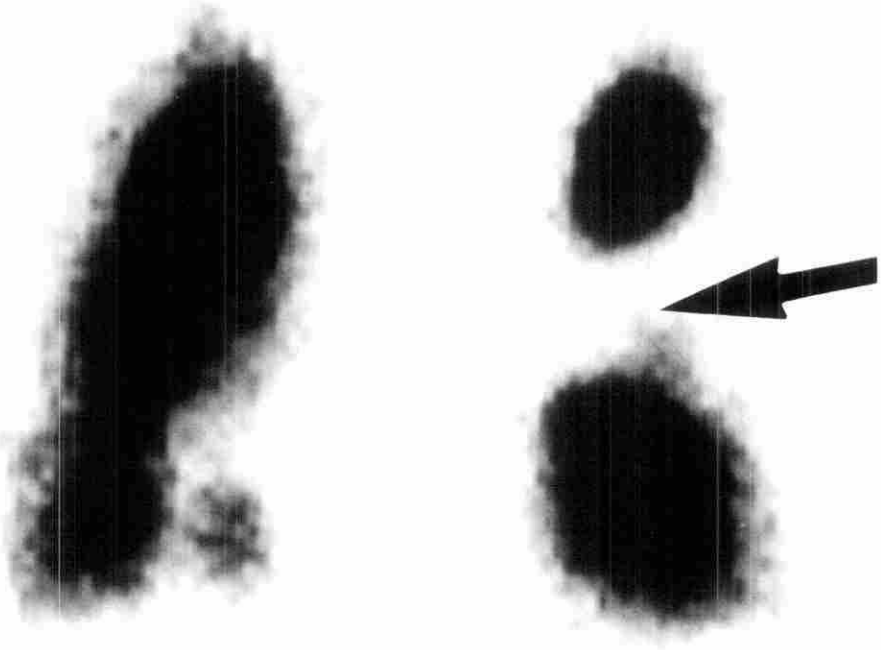

Fig. 3. The picture shows a typical Tc-99m DTPA radioaerosol distribution pattern with a significantly segmental defect in the middle portion of the right lung (arrow).

oaerssols were generated by a commercial lung aerosol delivery unit that allows convenient production of submicronic radioaerosols from self-contained, inexpensive nebulization systems. The particles of smaller size allow good penetrating and depositing in the peripherial portions of lungs. Since this test is simple and noninvasive, it may be used as a quantitative tool to assess the pharmacologic effect of fluticasone propionate inhalation therapy in children with asthma.

Inhaled corticosteroids have an important role in the treatment of chronic asthma in children [13]. Flucticasone propionate is a new inhaled corticosteroid for the treatment of asthma. The corticosteroids used as aerosols had the same desirable systemic effects as their oral counterparts because they were rapidly and efficiently absorbed through the mucous membrane. In addition, it has a potent glucocorticoid antiinflammatory action with few systemic effects [4]. Multiple mechanisms responsible for this beneficial effect of corticosteroid, such as fluticasone propionate, have been proposed as follows: antiinflammatory effects, delays and/or partially inhibits reaccumulation of intracellular histamine after discharge, reverses beta-adrenergic blockade, inhibits phosphodiesterase activity and increases intracellular cyclic AMP activity. In addition, it is reasonable to expect that corticosteroid shows favorable effects on mucociliary beats and mucous secretion in lung [1, 4, 7, 8].

Based on the preliminary findings, we can conclude that one-week of fluticasone propionate inhalation therapy may improve the bronchial obstruction in

Table 1. Detailed data of the changes on the homogeneity score over the bilateral lungs in children with asthma before and after one-week fluticasone propionate inhalation therapy

No.	Patient Sex	Age	Homogenesity score							
			Inhomogeneous distribution		Base to apex gradient		Segmental defects		Total scores	
			Pre-Tx	Post-Tx	Pre-Tx	Post-Tx	Pre-Tx	Post-Tx	Pre-Tx	Post-Tx
1	B	6	2	1	1	0	0	0	3	1
2	G	7	3	2	0	0	1	0	4	1
3	G	7	2	0	1	0	0	0	3	4
4	B	8	2	1	1	0	1	0	4	4
5	G	9	1	0	0	0	0	0	1	0
6	B	10	1	0	1	0	0	0	2	0
7	G	10	2	1	1	0	1	0	4	3
8	B	11	3	2	1	0	0	0	4	1
9	G	12	2	1	0	0	1	0	3	1
10	B	12	3	1	1	0	0	0	4	2
	Mean	9.2	2.1	0.9	0.7	0.0	0.4	0.0	3.2	1.7
	SD	2.1	0.7	0.7	0.5	0.0	0.5	0.0	1.0	1.5

B: boy, G: girl, Tx: one-week fluticasone propionate inhalation therapy, SD: standard deviation.

children with asthma by Tc-99m DTPA radioaerosol inhalation lung scintigraphy, which showed significantly decreased total homogeneity scores. However, further studies with more cases and longer time follow-up should be encouraged to confirm our preliminary findings.

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Accepted for publication: 28 March 2003