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# Tc-99m Technegas scintigraphy to evaluate the lung ventilation in patients with oral corticosteroid-dependent bronchial asthma

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Bronchial asthma is a clinical syndrome characterized by the reversibility of airway obstruction. Recently it has been suggested that remodeling of the airway causes irreversible airway obstruction which may be responsible for the patient's symptoms. With this background, the purpose of the present study was to assess patients with corticosteroid-dependent asthma by Tc-99m Technegas scintigraphy (Technegas) in both planar and SPECT images. Twelve patients (7 females and 5 males aged 36–72 years with a median age of 60 years: 4 smokers and 8 non-smokers) with oral corticosteroid-dependent asthma were enrolled in this study. Lung ventilation scanning with Technegas in both planar and SPECT images, high-resolution computed tomography, and pulmonary function tests were performed in all patients. The results of Technegas scanning were graded and correlations with other clinical parameters were evaluated. Significant abnormalities were detected by ventilation scintigraphy with Technegas in patients with corticosteroid-dependent bronchial asthma even during remission. Our data demonstrate that airflow obstruction took place in patients with corticosteroid-dependent asthma even during remission. Technegas scanning appears to be a useful radiopharmaceutical for demonstrating airflow obstruction in patients with bronchial asthma.

**Key words:** steroid dependent asthma, Tc-99m Technegas, ventilation scintigraphy, planar images, SPECT images, subepithelial fibrosis

## INTRODUCTION

BRONCHIAL ASTHMA is a clinical syndrome characterized by the reversibility of airway obstruction.[1] To treat bronchial asthma, inhalation therapy with corticosteroid and $\beta_2$-stimulants and anticholinergic agents is frequently used,[1] but in some patients oral corticosteroids are necessary to control their symptoms.[2] It has been suggested that in such patients remodeling of the airway causes irreversible airway obstruction which may be responsible for the patient's symptoms.[2] To evaluate an airway obstruction, the pulmonary function test and peak expiratory flow rate are routinely used.[1] To verify the remodeling of the airway histologically, bronchofiberscopy and biopsy of the bronchus are necessary,[2–4] but performing bronchofiberscopy and bronchial biopsy in patients with severe bronchial asthma is frequently difficult and sometimes dangerous.

To solve this problem, a new method to evaluate airway obstruction is required. Nowadays ultrafine Technetium-99m labeled carbon particles (Technegas) are being used for ventilation scintigraphy.[5–11] With this background, the purpose of the present study was to assess patients with corticosteroid-dependent asthma by Technegas scintigraphy by both planar and single photon emission CT (SPECT) images.

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## MATERIALS AND METHODS

### *Patients*

Table 1 shows the characteristics of 12 patients (7 females and 5 males aged 36–72 years with a median age of 60 years: 4 smokers and 8 non-smokers) enrolled in this study. The diagnosis of asthma was based on a history of wheezing or shortness of breath (or both) and the presence of variability of airflow obstruction, i.e., 20 percent improvement in $FEV_{1.0}$ within a period of a few months before the study. All of the subjects included in this study had some degree of irreversible airway obstruction during clinical remission from asthma, which was not reversed by intensive treatment including oral corticosteroid. None of the subjects had recent evidence of airway infection or an unstable respiratory condition within the 4 weeks preceding the study. The study was done in conformity with the Declaration of Helsinki and was approved by the Institutions Ethics Committees. All subjects gave their written informed consent. All patients received oral corticosteroid (5–10 mg/day). The history of bronchial asthma, levels of serum IgE, results of pulmonary function tests and peak expiratory flow rate (PEFR) are also shown in Table 1.

### *Bronchofiberscopy and bronchial biopsy*

Bronchial biopsy was performed in two patients (patients 8 and 9). Bronchofiberscopy was done according to standard procedures. Briefly, after local anesthesia of the throat, larynx, and bronchi with 2% and 4% lidocaine, a flexible bronchoscope was introduced into the bronchial tree. From each subject, biopsy specimens were taken from the carinae of lobar and segmental bronchi of the right lung with conventional forceps.

### *Technegas*[12–14]

Technegas was generated in a proprietary generator (Technegas Generator, Tetley Manufacturing Ltd., Sydney, Australia) by the resistive heating of a graphite crucible up to 2,500°C in which a saline solution of 505 MBq of Tc-99m pertechnetate was added and then the mixture was dried. After Technegas was generated in an atmosphere of 100% argon, it was dispersed in a lead-lined chamber. Following inhalation of 100% oxygen at 5 *l*/min for 3 minutes, all patients were given Technegas by inhalation through a mouthpiece while wearing a nose clip and lying in the supine position, while breathing as usual at the FRC level. After the administration of Technegas, planar imaging was performed in 6 projec-

**Table 1** Patient characteristics

| Case | Age & Sex | | History of asthma (year) | Smoking history | IgE (U/m*l*) | Percent vital capacity | $FEV_1$(%) | PEFR (L/min) | Oral prednisolone |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 62 | M | 2 | 2 packs/day for 30 years | NA | 79 | 58 | 300 | 5 mg |
| 2 | 45 | F | 2 | none | 23 | 56 | 88 | 300 | 5 mg |
| 3 | 65 | F | 6 | none | 55 | 82 | 68 | 200 | 10 mg |
| 4 | 36 | M | 10 | one pack/day for 20 years | 2000 | 99 | 71 | 500 | 10 mg |
| 5 | 57 | F | 5 | none | 33 | 85 | 78 | 250 | 5 mg |
| 6 | 69 | F | 2 | none | 230 | 74 | 72 | 250 | 5 mg |
| 7 | 61 | F | 7 | none | 330 | 106 | 69 | 300 | 5 mg |
| 8 | 72 | M | 30 | none | 470 | 76 | 63 | 240 | 10 mg |
| 9 | 47 | M | 1 | half pack/day for 27 years | 780 | 119 | 68 | 500 | 5 mg |
| 10 | 48 | F | 2 | none | 23 | 56 | 85 | 250 | 5 mg |
| 11 | 64 | M | 1 | half pack/day for 10 years | 610 | 96 | 69 | 450 | 5 mg |
| 12 | 64 | F | 8 | none | 100 | 70 | 76 | 300 | 5 mg |

NA: not available


**Fig. 1** Scores of the Technegas findings in planar images. A: grade 1, B: grade 2, C: grade 3

tions: anterior, posterior, right lateral, left lateral, right posterior oblique and left posterior oblique.

The SPECT system used was Picker model Prism 2000 (Northford, Connecticut, USA) with a low-energy, high-resolution collimator. The SPECT was rotated 360°. Seventy-two images were collected at 5° intervals for 40 seconds each with 128 × 128 matrix size. A low pass filter and a Ramp filter were used. No correction was made for attenuation. Each image was stored in a 128 × 128 pixel matrix. The axial images were compared with CT. The lower cut level of the display was 0% in planar images and 0–5% in SPECT images.

Three expert radiologists classified the Technegas findings in planar images into 3 grades according to the extent of inhomogeneous distribution and central hot spot formation: Grade 1, normal homogeneous distribution; Grade 2, peripheral heterogeneity; Grade 3, additional hot spot formation (Fig. 1). We also classified the Technegas findings in SPECT images into 4 grades according to the extent of peripheral irregularity and central hot spot formation: Grade 1, normal homogeneous distribution; Grade 2, peripheral heterogeneity; Grade 3, additional hot spot formation; and Grade 4, further regional defect (Fig. 2).

We performed the Technegas examination in 10 normal volunteers (all non-smokers) as a control, and results were all grade 1 for both planar and SPECT images.

*High-resolution computed tomography (HRCT)*

HRCT was performed by making 12 slices from above the aortic arch to the diaphragm with 5 mm collimation in a bone detail algorithm during moderate inspiration with two CT scanners, CT9800 and HiSpeed Advantage (General Electric, Milwaukee, Wisconsin, USA). HRCT images from each lung were displayed with a window level of −600 and a window width of 1,500.

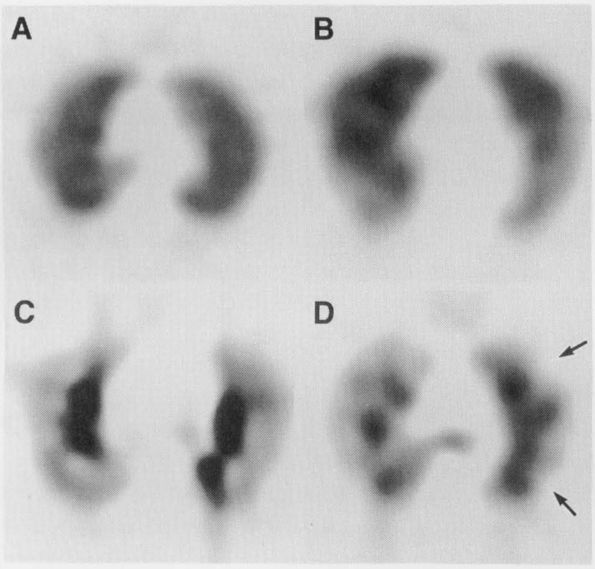


**Fig. 2** Scores of the Technegas findings in SPECT images. A: grade 1, B: grade 2, C: grade 3, D: grade 4. Note regional defects in the grade 4 (arrows).

**Fig. 3** Light microphotographs of bronchial biopsy specimens of patients with corticosteroid-dependent asthma. Subepithelial fibrosis is clearly demonstrated (arrows).

**Table 2** Results of scintigraphy

| Case | HRCT | Technegas planar | | Technegas SPECT | |
|---|---|---|---|---|---|
| | | Pattern | Grade | Pattern | Grade |
| 1 | normal | inhomogeneous | 2 | inhomogeneous | 2 |
| 2 | normal | normal | 1 | normal | 1 |
| 3 | normal | normal | 1 | normal | 1 |
| 4 | normal | hot spot | 3 | hot spot | 3 |
| 5 | normal | inhomogeneous | 2 | inhomogeneous/hot spot | 3 |
| 6 | normal | inhomogeneous | 2 | inhomogeneous | 2 |
| 7 | normal | normal | 1 | inhomogeneous | 2 |
| 8 | normal | inhomogeneous/hot spot | 3 | hot spot/defect | 4 |
| 9 | normal | inhomogeneous | 2 | inhomogeneous/hot spot | 3 |
| 10 | normal | normal | 1 | inhomogeneous | 2 |
| 11 | normal | normal | 1 | normal | 1 |
| 12 | normal | normal | 1 | inhomogeneous | 2 |

## RESULTS

Table 2 shows the results of HRCT and planar as well as SPECT images according to Technegas grades in patients with corticosteroid-dependent bronchial asthma. No patients demonstrated abnormality in HRCT. In the planar images, 6 patients were judged as grade 1; 4 patients as grade 2 and 2 patients as grade 3. In SPECT images, 3 patients were judged as grade 1; 5 patients as grade 2; 3 patients as grade 3 and 1 patient as grade 4. Pathological findings of bronchial biopsy obtained from patient 8 (Fig. 3) and patient 9 demonstrated significant subepithelial fibrosis.

## DISCUSSION

In the present study we demonstrated that significant abnormalities were detected by ventilation scintigraphy with Technegas in patients with corticosteroid-dependent bronchial asthma even during remission.

The Technegas scan was technically simple to perform and was well tolerated by the patients. Technegas is ultrafine carbon particles of the order of 0.005 μm.[6,9] Since particles of Tc-99m phytate aerosol are larger than 2 μm, and are likely to be deposited in the proximal bronchial trunks, Technegas images are very useful in cases of severe chronic obstructive pulmonary disease.[12] The image quality is also superior to Xenon-133 gas because of the improved resolution at the edges of the lungs and the availability of multiple views.[11] In addition, it has been reported that Technegas SPECT imaging also gives more detailed diagnostic information on lung ventilation imaging than planar images.[12–15] Satoh et al. reported the usefulness of Technegas SPECT to diagnose pulmonary emphysema.[12–14] In addition, Zhang et al. reported that an index expressing the subliminal heterogeneous distribution by Technegas SPECT correlates well with the severity of silicosis.[15]

There are however, no reports which evaluate the usefulness of Technegas to diagnose bronchial asthma. Before evaluating the images of Technegas in patients with bronchial asthma, the effects of complicated asthma attacks should be discussed. In our study, all of the patients received a one week treatment with oral prednisolone (30 mg/day) and used BDP regularly before the examination, so that none of the patients had an asthma attack during the seven days of treatment or during the Technegas examination.

There has also been much confusion in distinguishing chronic asthma from emphysema in patients with airway obstructive diseases because of their similar clinical symptoms and the possibility of coexistence.[16] The evaluation of emphysematous change in chronic asthma in relation to the effect of cigarette smoking is clinically important especially in smokers.[16] In our study, to exclude the possibility of complicated pulmonary emphysema especially in smokers, HRCT was performed in all patients and confirmed that there was no low attenuation area in the lung fields, so that the results for Technegas precisely reflected the airflow of patients with oral corticosteroid-dependent bronchial asthma.

Interestingly, abnormal findings for Technegas were frequently observed, suggesting that irreversible airway obstruction took place in patients with corticosteroid-dependent bronchial asthma. Importantly, deposition of Technegas in central airways was frequently observed.

The intrapulmonary deposition of inhaled particles is determined by inertial impaction, gravitational settling and Brownian diffusion.[8] The principal factor determining particle deposition, the mechanism responsible and the site within the lung, is the particle size.[17,18] Whereas aerosol images formed of particles with a diameter less than 2 μm do not show preferential central deposition compared with true gas in normal subjects, aerosols with particles as small as 0.12 μm have consistently shown preferential central deposition in patients with severe airway obstruction.[17,18] Presumably this is a consequence of marked reduction in the diameter of proximal airways in such subjects, increasing the inertial impact of even submicronic particles.[8] In addition, in most of these studies there is increased inhomogeneity of aerosol distribution extending out to the lung periphery.[17–19] Such patterns have been attributed to localized impact of aerosol particles in relatively peripheral airways which are grossly narrowed and/or distorted.[8]

On theoretical grounds, hot spots can arise at airway bifurcations or in areas of non-stable flow.[9] Arnot et al. noted hot spots in a number of patients with airway disease.[7] They postulated that there are small regions of lung in which airways are almost completely obstructed and into which particles can drift by diffusion, deposit and accumulate further with each inspiration/expiration cycle.[7] Central/large airway deposition can arise as a direct consequence of narrowing of the large airways but may also result from altered ventilatory flow due to small/peripheral airway disease or changes in compliance within peripheral lung units.[9] Partial obstruction of a bronchus will lead to increased flow through neighboring bronchi and increased particle deposition caused by impact as well as localized deposit at the site of the obstruction.[5] Various degrees of obstruction may arise from factors such as smooth muscle constriction, submucosal edema or inflammation and mucous hypersecretion with mucous plugging or formation of mucoid strands.[9] Wenzel et al. reported that inflammation remains in severe symptomatic asthmatics despite treatment with large doses of glucocorticoids.[2] In agreement with these lines of evidence, subepithelial fibrosis was clearly observed in bronchial biopsy specimens obtained from 2 patients.

In conclusion, our data demonstrate that airflow obstruction might take place in patients with corticosteroid-dependent asthma even during remission. Technegas scintigraphy appears to be a useful radiopharmaceutical for demonstrating airflow obstruction in patients with bronchial asthma.

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