Nuclear Medicine & Biology, Vol. 27, pp. 215–218, 2000

ISSN 0969-8051/00/$–see front matter
PII S0969-8051(99)00102-X

^{99m}Tc-ENS Ventilation Scintigraphy: Preliminary Study in Human Volunteers

G. Calmanovici,[1] J. Boccio,[1] C. Goldman,[1] A. Hager,[2] T. De Paoli,[2] M. Alak,[3] O. Degrossi,[3] H. García del Río,[3] J. Nicolini,[4] R. Caro[1] and M. Zubillaga[1]

[1]RADIOISOTOPE LABORATORY, SCHOOL OF PHARMACY AND BIOCHEMISTRY, UNIVERSITY OF BUENOS AIRES, BUENOS AIRES, ARGENTINA; [2]PHYSICS DEPARTMENT, SCHOOL OF PHARMACY AND BIOCHEMISTRY, UNIVERSITY OF BUENOS AIRES, BUENOS AIRES, ARGENTINA; [3]ARGENTINE INSTITUTE OF DIAGNOSIS AND TREATMENT, BUENOS AIRES, ARGENTINA; AND [4]BACON LABORATORIES, BUENOS AIRES, ARGENTINA

ABSTRACT. Exogenous natural surfactant (ENS) labeled with ^{99m}Tc (^{99m}Tc-ENS, 900–1110 MBq), a new radiopharmaceutical for ventilation scintigraphy, was nebulized during 3 min to five volunteers. For comparative purposes, ^{99m}Tc-diethylenetriamine pentaacetic acid (DTPA) was studied in the same way. ^{99m}Tc-ENS images were of at least the same quality as ^{99m}Tc-DTPA images. However, in smoking volunteers, the ^{99m}Tc-DTPA images show some areas that seemed to be not well-ventilated, although these areas appeared well-ventilated when the study was performed with ^{99m}Tc-ENS. These results suggest that ^{99m}Tc-ENS can be used for ventilation scintigraphy to allow the observation of some areas that cannot been visualized using ^{99m}Tc-DTPA as ventilation agent. NUCL MED BIOL 27;2:215–218, 2000. **© 2000 Elsevier Science Inc. All rights reserved.**

KEY WORDS. Ventilation scintigraphy; ^{99m}Tc-ENS; Surfactant; Lung; ^{99m}Tc

INTRODUCTION

Aerosol lung scintigraphy is a very important tool for the diagnosis of pulmonary thromboembolism (10, 13, 14, 19) as well as other ventilatory related abnormalities (3, 9). Several agents can be used for this scintigraphic study. Each nuclear medicine center chooses an agent according to an analysis of the advantages, disadvantages, and functional information given by each ventilatory radiopharmaceutical. The various agents currently in use for ventilation scintigraphy are still being studied so as to determine the optimal radiopharmaceutical. ^{133}Xe, ^{81m}Kr, and ^{99m}Tc-labeled aerosols are the most widely used radiopharmaceuticals for ventilation scintigraphy. The drawbacks of ^{133}Xe and ^{81m}Kr are well known (2, 16, 17). Technegas® is being used for ventilation scintigraphy in several countries (11, 15). However, nuclear medicine centers in developing countries cannot afford to purchase the Technegas equipment. In Argentina, as well as in other developing nations, ^{99m}Tc-diethylenetriamine pentaacetic acid (DTPA) is used in the majority of the ventilation scintigaphic studies, although this agent is not specific for the lung (6).

For these reasons, our laboratory is studying a new radioaerosol for ventilation scintigraphy, the exogenous natural surfactant (ENS) labeled with ^{99m}Tc (^{99m}Tc-ENS) (4–6). Previous studies demonstrated that the labeling yield percentages obtained for ^{99m}Tc-ENS were always >95% (5, 6). The percentage of activity concentration found in lungs for ^{99m}Tc-ENS was >90% in previous studies performed in an animal model (4, 5), indicating the high specificity of this radiopharmaceutical for the lungs. We present here the results of the first study in human volunteers of ^{99m}Tc-ENS as ventilation agent.

Address correspondence to: Gabriela Calmanovici, Biochemist, Radioisotope Laboratory, School of Pharmacy and Biochemistry, University of Buenos Aires, Junín 956, 1113-Buenos Aires, Argentina; e-mail: gcalmano@huemul.ffyb.uba.ar.

Received 6 March 1999.
Accepted 20 November 1999.

MATERIALS AND METHODS

Study Population

The Ethical Committee of the Argentine Institute of Diagnosis and Treatment approved the study according to the 1964 Declaration of Helsinki. All persons gave informed consent prior to inclusion in the study. Five healthy asymptomatic volunteers (two men, three women) between the ages of 25 and 58 years were studied. Two volunteers were smokers who smoked between 10 and 20 cigarettes per day; the rest were nonsmokers.

Procedure

$^{99m}TcO_4^-$ was eluted from a molybdenum generator (Bacon Laboratories, Ultra-Technekow FM, Argentina; activity: 3,700 MBq) as sodium pertechnetate, which was used for labeling the radiopharmaceuticals.

To obtain the ^{99m}Tc-ENS, 2.5 mg of freeze-dried ENS (freeze-dried Baby Fact P/GEMEPE SA, Argentina) (5) were labeled with ^{99m}Tc (^{99m}Tc-ENS), using stannous fluoride (Sigma Chemical Co., St. Louis, MO USA) as a reducing agent (6). Of this ^{99m}Tc-ENS suspension, 925–1,110 MBq were placed in an Ultra Vent kit (Bacon Laboratories, Argentina) to be aerosolized. The volunteer then inhaled the aerosol for 3 min through a mouthpiece with a noseclip in place. A one-way valve was used to discharge the exhaled gas and droplets into a shielded trap.

Seven days after the ^{99m}Tc-ENS study, ventilation scintigraphy with ^{99m}Tc-DTPA was performed with the same equipment in the same group of volunteers. The ^{99m}Tc-DTPA was obtained labeling the DTPA sodium salt (Bacon Laboratories) with ^{99m}Tc. Of this solution, 999–1,110 MBq were placed in the chamber of the

Table 1. Individual Data and Mean ± SD for the Administered Activity and the Acquisition Times for the Images Obtained with ^{99m}Tc-ENS and ^{99m}Tc-DTPA

		^{99m}Tc-ENS			^{99m}Tc-DTPA		
			Acquisition time			Acquisition time	
Patient no.	S	Adm Act (MBq)	5 (min)	15 (min)	Adm Act (MBq)	5 (min)	15 (min)
[a]1	N	1,014	1.70	1.77	1,003	0.52	0.55
[b]2	N	936	1.95	1.71	999	1.33	1.3
[a]3	N	1,129	1.15	1.17	1,047	1.57	1.6
[b]4	Y	1,110	0.33	0.35	1,099	1.07	1.02
[b]5	Y	1,043	1.05	1.33	999	1.25	1.28
Mean		1,046	1.236	1.266	1,029	1.148	1.150
SD		78	0.630	0.571	44	0.394	0.393

Aquisition times 5 and 15 are the acquisition times for the images acquired 5 min and 15 min after the nebulization procedure, respectively.
[a]Male; [b]female.
S, smoker, N, no; Y, yes; Adm Act, administered activity; ENS, exogenous natural surfactant; DTPA, diethylenetriamine pentaacetic acid.

nebulizer to be administered to the volunteers in 3 min ventilation time. In both cases quality control of the radiopharmaceutical was performed by an ascending paper chromatography using acetone (Merck, Germany) as solvent (5–7).

Image Acquisition

The images were obtained with a single photon emission computed tomography camera (Siemens Diacam, USA) connected to a computer (Graphic Series G800, View Sonic, USA). The computer program used was ICON 7.1 (Siemens, USA). Counts were accumulated up to 100 Kc. Images were acquired 5 and 15 min after the nebulization procedure for each radiopharmaceutical. They were compared by two independent experienced nuclear medicine observers in a blind test analysis and classified according to image quality.

Results obtained for acquisition times are given as mean ± SD

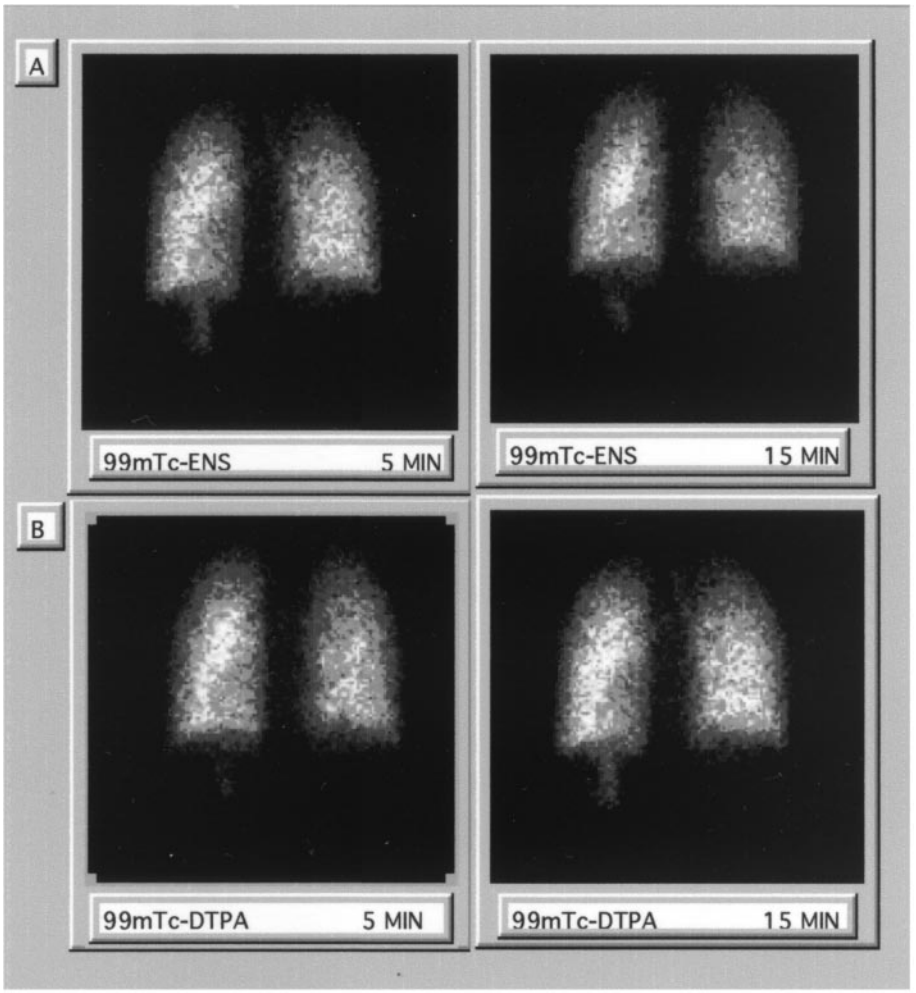

FIG. 1. Images of a nonsmoking volunteer (volunteer no. 2) 5 and 15 min after the nebulization of (A) 936 MBq of exogenous natural surfactant labeled with ^{99m}Tc (^{99m}Tc-ENS) and (B) 999 MBq of ^{99m}Tc-diethylenetriamine pentaacetic acid (DTPA). Nebulization time: 3 min.

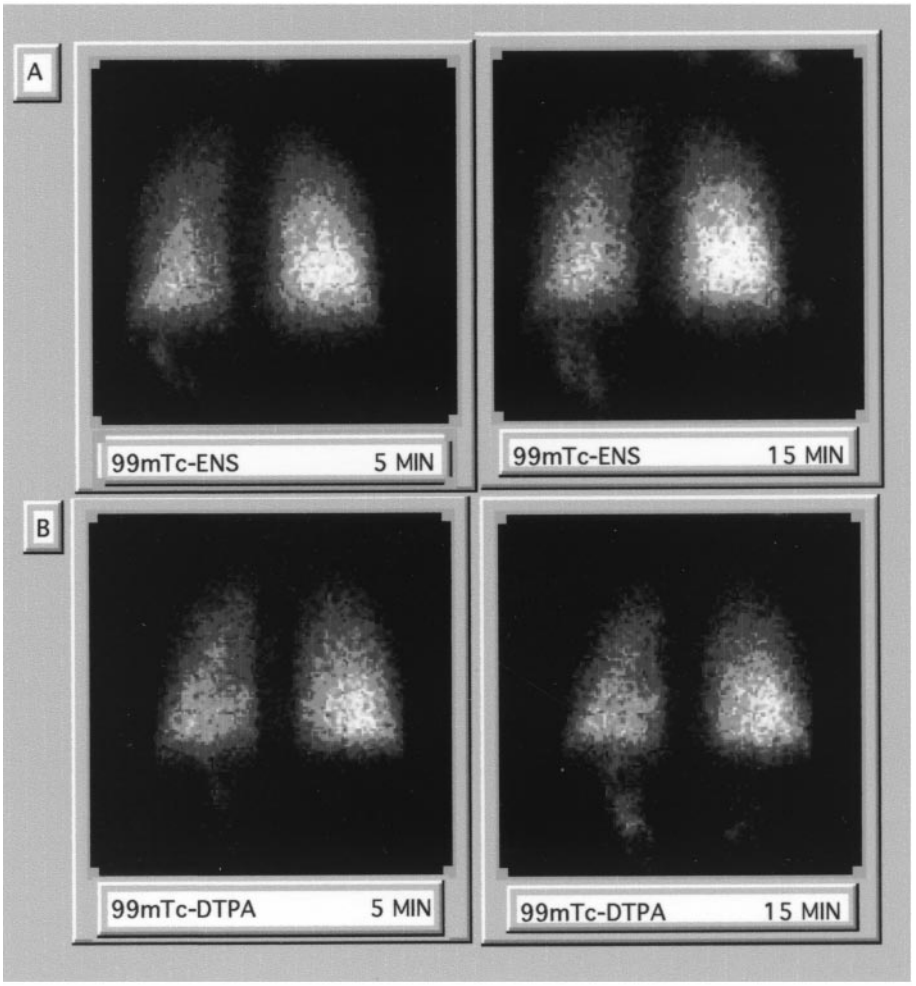

FIG. 2. Images of a smoking volunteer (volunteer no. 4) 5 and 15 min after the nebulization of (A) 1,110 MBq of exogenous natural surfactant labeled with ^{99m}Tc (^{99m}Tc-ENS) and (B) 1,099 MBq of ^{99m}Tc-diethylenetriamine pentaacetic acid (DTPA). Nebulization time: 3 min.

and were evaluated by two-factor experiment with repeated measures on one factor. A *p*-value of 0.05 was considered significant (8).

RESULTS

The labeling yield percentages were always >99% for ^{99m}Tc-ENS as well as for ^{99m}Tc-DTPA.

In Table 1 the individual data as well as the mean ± SD for the administered activity and acquisition times for each radiopharmaceutical are shown. There was no significant difference between the acquisition times for the images obtained with each radiopharmaceutical 5 and 15 min after the nebulization procedure.

Figure 1 shows the images obtained with ^{99m}Tc-ENS (Fig. 1A) and ^{99m}Tc-DTPA (Fig. 1B) for an healthy, asymptomatic nonsmoking volunteer. It can be observed that the images obtained for ^{99m}Tc-ENS were of at least the same quality as those obtained with ^{99m}Tc-DTPA. In the rest of the healthy, asymptomatic nonsmoking volunteers the images were similar to the ones shown in Figure 1. The images for a healthy, asymptomatic smoking volunteer are shown in Figure 2. It can be observed that the images obtained for the same volunteer show areas that seem to be not well-ventilated in the ^{99m}Tc-DTPA images (Fig. 2B). These same areas appear well-ventilated when ^{99m}Tc-ENS was used as the ventilation agent (Fig. 2A). This difference is more evident in the 15-min acquisition time image. In the other studied healthy, asymptomatic smoking volunteers the images obtained were similar to those shown in Figure 2.

DISCUSSION

^{99m}Tc-ENS was evaluated as an agent for ventilation scintigraphy compared with ^{99m}Tc-DTPA. The images obtained with this new radiopharmaceutical were of at least the same quality as the ^{99m}Tc-DTPA images with homogenous distribution patterns (Figs. 1 and 2) and a reasonable acquisition time (Table 1). In Figure 1 it can be observed that there was no difference between radiopharmaceuticals in asymptomatic nonsmoking volunteers. Alternatively, in healthy, asymptomatic smoking volunteers, there are some areas in the ^{99m}Tc-DTPA images that seem to be not well-ventilated (Fig. 2B), whereas when ^{99m}Tc-ENS was used these areas appear as well-ventilated (Fig. 2A). This is more evident in the 15-min images. This can be explained by the fact that ^{99m}Tc-DTPA clearance is increased in smokers as well as in patients with other abnormalities in which the alveolar-blood membrane is injured (1, 12, 18), whereas ^{99m}Tc-ENS remains in the lung for at least for 30 min after the nebulization procedure, as has been demonstrated in animal studies (5, 6). This may be due to the incorporation of ENS into the surfactant layer that lines the alveoli. These results suggest that in smokers it is quite difficult to diagnose ventilatory related abnormalities or pulmonary thromboembolism, because areas with increased ^{99m}Tc-DTPA clearance can be confused with areas that are not well-ventilated. Conversely, when ^{99m}Tc-ENS is used as ventilatory agent, these areas appeared well-ventilated, which seems to confirm the specificity of this radiopharmaceutical for the alveolar surfactant layer.

Another important point to consider is the time between the nebulization procedure and the image acquisition. When the image is not acquired immediately after the nebulization in a smoking volunteer, the quality of ^{99m}Tc-DTPA images is not the same as that obtained immediately after the nebulization. This can be observed comparing the 5 and 15 min images (Fig. 2B). On the other hand, ^{99m}Tc-ENS image quality was the same whether it was acquired 5 min or 15 min after the nebulization procedure (Fig. 2A). Moreover, the percentage of activity concentration in the lungs of rats 30 min after nebulization of ^{99m}Tc-ENS was >90% (5, 6), suggesting that the image can be taken at least 30 min after this procedure without any loss of quality.

Studies in several patients with different pathologies using ^{99m}Tc-ENS as a ventilation agent are currently being performed. The results of these studies will be shown in future studies.

CONCLUSION

^{99m}Tc-ENS can be used successfully for ventilation scintigraphy. The results obtained suggest that it would be especially useful when the alveolar-blood barrier is injured such as it is smokers. In these cases it is very difficult to diagnose a ventilatory related abnormality or pulmonary thromboembolism using ^{99m}Tc-DTPA as a ventilation agent because areas with increased ^{99m}Tc-DTPA clearance are confused with areas that are not well-ventilated. In the case of ^{99m}Tc-ENS this problem is not observed.

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