EVALUATION OF MALIGN LUNG LESIONS WITH Tc-99m TETROFOSMIN IN COMPARISON TO THALLIUM-201 AND Tc-99m MIBI RESULTS

Tc-99m Tetrofosmin ile malign akciğer lezyonlarının değerlendirilmesi; thallium-201 ve Tc-99m MIBI sonuçları ile karşılaştırma

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Summary: *The aim of this study was to investigate the diagnostic role of Tc-99m-tetrofosmin in malign lung lesions and to compare the results with Tc-99m hexakis 2-methoxyisobutylisonitrile (Tc-99m MIBI) and Tl-201. This study was carried out on twenty-six patients (23 males, three females, mean age ± SD 62.4±8.9 yr) with primary bronchial carcinoma (14 epidermoid carcinoma, eight small cell carcinoma, two adenocarcinoma, two undifferentiated large cell carcinoma). The images were evaluated visually and also semiquantitatively. Lesion/contralateral normal lung (L/NL) ratios were calculated 30 minutes after the injection of 740 MBq ^{99m}Tc-tetrofosmin, ^{99m}Tc-MIBI, and 180 minutes after the injection of 111 MBq ^{201}Tl. While MIBI and tetrofosmin studies had two false negative results, there were three false negative results for ^{201}Tl study. The mean tumor uptake ratios of ^{99m}Tc-tetrofosmin, ^{99m}Tc-MIBI and ^{201}Tl were 1.41±0.025, 1.47±0.023, 1.69±0.20 respectively. The L/NL ratio was slightly higher with ^{99m}Tc-MIBI and ^{201}Tl than ^{99m}Tc-tetrofosmin, however ^{99m}Tc-MIBI and ^{99m}Tc-tetrofosmin appears same sensitivity in the detection of malign lung lesions. For this reason we concluded that tetrofosmin is a promising agent in the evaluation of malign lung lesions.*

Key Words: *Bronchial carcinoma, Tc-99m tetrofosmin, Tc-99m MIBI, Tl-201*

Özet: *Bu çalışmanın amacı, malign akciğer lezyonlarında Tc-99m-tetrofosmin'in tanısal değerini araştırmak ve Tc-99m-MIBI ve Tl-201 sonuçları ile karşılaştırmaktır. Çalışmaya, primer bronş kanseri olan (ondört epidermoid karsinom, sekiz küçük hücreli karsinom, iki adeno karsinom, iki indiferansiye büyük hücreli karsinom), üçü kadın yirmiüçü erkek (ortalama yaş 62.4 ± 8.9 yıl) olmak üzere toplam yirmialtı hasta dahil edildi. Filmler hem vizüel hem de semikantitatif olarak değerlendirildi. 740 MBq ^{99m}Tc-tetrofosmin ve ^{99m}Tc-MIBI enjeksiyonundan 30 dakika sonra, 111 MBq ^{201}Tl enjeksiyonundan ise 180 dakika sonra, lezyon/normal akciğer (L/NL) oranları hesaplandı. Tc-99m tetrofosmin ve ^{99m}Tc-MIBI ile yapılan çalışmada iki yanlış negatif sonuç mevcutken, ^{201}Tl ile yapılan çalışmada üç yanlış negatif sonuç mevcuttu. Ortalama tumor uptake oranları ^{99m}Tc-tetrofosmin, ^{99m}Tc-MIBI ve ^{201}Tl için sırasıyla 1.41±0.025, 1.47±0.023 ve 1.69±0.20 olarak bulundu. Tc-99m MIBI ve ^{201}Tl ile elde edilen L/NL oranı ^{99m}Tc-tetrofosmin ile elde edilen orandan biraz yüksek bulundu. Bununla birlikte, malign akciğer lezyonlarının tesbitinde ^{99m}Tc-tetrofosmin ve ^{99m}Tc-MIBI'nin eşit sensitiviteye sahip olduğu görüldü. Bu nedenle, malign akciğer lezyonlarının değerlendirilmesinde tetrofosmin'in umut verici bir ajan olduğu sonucuna varıldı.*

Anahtar Kelimeler: *Bronş kanseri, Tc-99m tetrofosmin, Tc-99m MIBI, Tl-201*

Introduction

Appropriate treatment of the patients with bronchial carcinoma is required diagnostic imaging methods for staging, monitoring of the treatment, determining optimum timing for definitive surgical procedures, and early detection of recurrence. Although patients with lung cancer are routinely evaluated with anatomic imaging modalities such as computed tomography (CT) or magnetic resonance (MR) imaging, some radiopharmaceuticals such as ^{201}Tl, ^{99m}Tc-MIBI, ^{99m}Tc-tetrofosmin have the ability to localize in viable cells of tumors, that allows the differential diagnosis among post-therapy changes, residual

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viable tumor tissue, local recurrence, or necrosis (1-5). The importance of these radiopharmaceuticals in the evaluation of tumor viability and in the differentiation of the lesions as benign or malign is increasing because of the problems encountered by MR imaging and CT scan (6).

Thallium-201 is a monovalent cation like potassium, and mainly accumulated by viable tumor, less so by connective tissue, and barely detectable in necrotic tissue (7,8). This agent has achieved widespread acceptance in clinical oncologic imaging, but well known some problems of this agent are significant disadvantages. This radiopharmaceutical is a familiar tumor imaging agent in patients with lung cancer, Hodgkin's lymphoma, bone tumor, and thyroid carcinoma (9-12). Tl-201 is reported to have a multifactorial mechanism of tumor uptake, i.e.; blood flow, viability, tumor type, sodium-potassium ATPase system, co-transport system, calcium ion channel exchange, vascular immaturity with leakage, and increased cell membrane permeability (13). Because ^{201}Tl has some well-known limitations, the new tumor-seeking agents that can be labeled with ^{99m}Tc are being investigated.

Both hexakis (2-methoxyisobutyl isonitrile) technetium (I) (^{99m}Tc-sestamibi) and ^{99m}Tc-tetrofosmin are the lipophilic cationic organotechnetium compounds developed for myocardial perfusion imaging (5,14). These compounds use the more favorable physical advantages of ^{99m}Tc for applications in clinical imaging. Tetrofosmin can be labelled with ^{99m}Tc at room temperature as compared to sestamibi which required heating for approximately 20 minutes. The aim of our study was to investigate the diagnostic role of ^{99m}Tc tetrofosmin in malign lung lesions and to compare the results with ^{99m}Tc-MIBI and ^{201}Tl.

Materials and methods

Twenty-six patients (twenty three males and three females, mean age 62.4±8.9 yr with primary bronchial carcinoma were included in our study. All patients gave their informed consent prior to the study. Of the patients, fourteen had epidermoid carcinoma, eigth small cell carcinoma, two adenocarcinoma, and two undifferentiated large cell carcinoma. None of the patients had received therapy (radio/chemotherapy) before the study. All patients had also a plain chest X-ray graphy and CT scan. Final diagnosis of bronchial carcinoma was obtained with bronchoscopic biopsy (n=17) and surgical specimen (n=9).

Tc-99m tetrofosmin (Myoview, Amersham International, England) and ^{99m}Tc-MIBI (Cardiolite, Du Pont Company) was prepared according to the product information. Thin-layer chromatography was used to control radiochemical purity, and the radiopharmaceuticals were used if the purity was ≥ 90 %.

All images were obtained using a rotating gamma camera (Toshiba GCA 602 A/SA, Tokyo, Japan, and Starcam 4000i, GE Medical Systems) fitted with a low-energy general purpose collimator. Planar images (256 word matrix) of the anterior chest were initiated 30 min after the injection of 740 MBq ^{99m}Tc-tetrofosmin and ^{99m}Tc-MIBI, and 180 min after the injection of 111 MBq ^{201}Tl. The imaging duration is five min for ^{99m}Tc-tetrofosmin and ^{99m}Tc-MIBI, and seven min for ^{201}Tl. These images were interpreted both qualitatively and semiquantitatively. First, the images were visually evaluated for focal uptake in the tumor mass. Next, tumor uptake ratios were calculated by using ROI drawn on lesion and contralateral normal lung.

Statistical comparisons were made by One Way Analysis of Variance. P value less than 0.05 was considered to be statistically significant.

Results

Visual evaluation

Of the patients, twenty-four showed ^{99m}Tc-MIBI and ^{99m}Tc-tetrofosmin uptake, and twenty-three ^{201}Tl uptake. The sensitivity in the detection of primary tumor was 92.3% for ^{99m}Tc-MIBI and ^{99m}Tc-tetrofosmin imaging, and 88.5% for ^{201}Tl imaging. In two patients with epidermoid carcinoma, the lesions coult not be identified by

both ^{99m}Tc-tetrofosmin and ^{99m}Tc-MIBI imaging. However, in three patients (two epidermoid carcinoma and one small cell carcinoma), the tumors could not be also visualized by ^{201}Tl imaging. The patient who showed focal uptake pattern by the three agents were seen on Figure 1.

Semiquantitative analysis

The lesions were also evaluated semiquantitatively. Lesion/contralateral normal lung (L/NL) ratios were calculated for the three radiopharmaceuticals. The mean tumor uptake ratio (TUR) values of ^{99m}Tc-tetrofosmin, ^{99m}Tc-MIBI and ^{201}Tl were 1.41±0.025, 1.47±0.023, 1.69±0.200 respectively (Table 1). The difference among the TUR values for the histologic type of the tumor by the three agents was not significant (p>0.05), suggesting that these agents cannot achieve the differential diagnosis among the histologic types of the tumors.

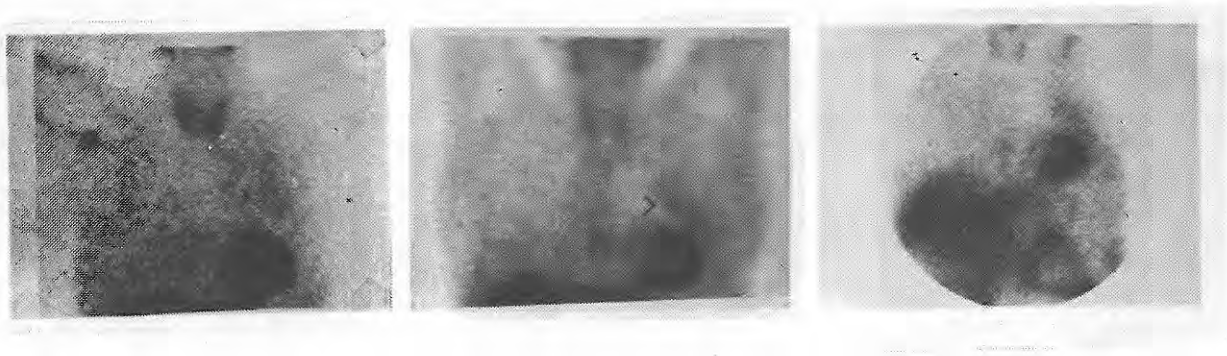

Fig 1. The patient who showed focal uptake pattern in the left lung by (a) Tc-99m-tetrofosmin, (b) Tc-99m-MIBI, and (c) T1-201

Table 1. The mean tumor uptake ratio values of ^{99m}Tc-tetrofosmin, ^{99m}Tc-MIBI, and ^{201}Tl.

	n	Mean±SEM
^{99m}Tc-tetrofosmin	36	1.41 ± 0.025
^{99m}Tc-MIBI	36	1.47 ± 0.023
^{201}Tl	36	1.69 ± 0.200
		p>0.05

Discussion

In the last two decades there have been rapid developments in the imaging modalities. Accurate staging of the malign lesions is essential to achieve the most appropriate treatment. Various nuclear or nonnuclear imaging techniques compete with or complement one another in this subject. Nonnuclear imaging techniques including the plain chest X-ray, CT scan and MRI are the most cost-effective screening and diagnostic procedures in the evaluation of lung cancer (15). However, none of these procedures has been proven to be accurate enough to evaluate the lung tumor. Tl-201 has shown that thallium uptake in tumors reflects the presence of underlying viable tumor tissue more accurately than do other radionuclides (16). Unfortunately, ^{201}Tl studies in tumors suffer from lack of specificity due to occasional ^{201}Tl uptake in benign lesions (17,18). Since well-known disadvantages of ^{201}Tl in compared with ^{99m}Tc, the researches on the new ^{99m}Tc labeled agents have gained a particular importance. For this purpose, many studies have been made to find a tumor imaging agent that can be labeled with ^{99m}Tc which is available at any time and has the excellant nuclear properties of ^{99m}Tc. Technetium-99m has a high energy level and a shorter physical half life than ^{201}Tl allowing larger intravenous injection doses. The tumor uptake mechanism of ^{99m}Tc-MIBI is not yet clearly understood. However, various uptake mechanisms have been suggested. It binds to the cytosol in the tumor cell, and therefore there is no influx or outflux after the initial uptake (19). The cationic charge and lipophilicity of ^{99m}Tc-MIBI, the mitochondrial and plasma membrane potentials of the tumor cell, and the cellular mitochondrial content may play an important role in the tumor uptake of this agent (20-23). The late intracellular concentration of ^{99m}Tc-MIBI has been found to be inversely related to the degree of expression of permeability (P) glycoprotein that responsible for the development of multidrug resistance to chemotherapeutic agents (24). Tc-99mMIBI and ^{99m}Tc-tetrofosmin have some similar properties (25,26). This agent has also been searching for its potential about tumor imaging. So far, a few study was reported about tumor imaging for this agent (27-29).

In our study, the L/NL ratio was slightly higher with ^{99m}Tc-MIBI and ^{201}Tl than ^{99m}Tc-tetrofosmin, however ^{99m}Tc-MIBI and ^{99m}Tc-tetrofosmin appears same sensitivity in malign lung lesions. For this reason we concluded that tetrofosmin is a promising agent in the evaluation of malign lung lesions, and none of these three agents can differentiate among the histologic types of the tumors.

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