Comparative Study Between $^{99m}$Tc-MDP and $^{99m}$Tc-DTPA as a Predictor For Renal Function

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Abstract: Renal scintigraphy can provide the valuable split renal function which is not obtainable by other non-invasive measurements. This study was designed to investigate the feasibility of the assessment of relative renal function with $^{99m}$Tc-MDP as compared with renal imaging radiotracers used for that purpose. Differential renal function i.e. the contribution of percent that each kidney makes to global renal function was determined prospectively in 35 patients (23 males, 12 females, mean age 47±14y) using $^{99m}$Tc-MDP and a renal radionuclide tracer $^{99m}$Tc-DTPA. Differential function was computed in all cases from the early (1-3 minutes) renal uptake of the tracers by Region Of Interest analysis (ROI) of the computer acquired data. There was a high correlation between values of differential renal function obtained with $^{99m}$Tc-MDP and those obtained with $^{99m}$Tc-DTPA ($r=0.98$, $P<0.0001$). Total glomerular filtration rate, split glomerular filtration rate and renograms time to peak activity derived from both tracers were also highly correlated ($r=0.96$, $P<0.0001$), ($r=0.98$, $P<0.0001$) and ($r=0.97$, $P<0.0001$), respectively. It is concluded that the characteristics of renal handling of $^{99m}$Tc-MDP were similar to those of $^{99m}$Tc-DTPA so that accurate estimation of differential renal function are possible with this agent, and that $^{99m}$Tc-MDP determined renal function most likely reflects differential glomerular filtration rate.

Key words: $^{99m}$Tc-DTPA, $^{99m}$Tc–MDP, GFR, Scintigraphy, Modification of Diet in Renal Disease, Cockcroft-Gault.

INTRODUCTION

Technetium-99m-Diethylene TriaminePenta Acetic acid ($^{99m}$Tc-DTPA) is a chelating agent which was introduced into renal nuclear medicine in 1970. $^{99m}$Tc-DTPA is the least expensive renal radiopharmaceutical. It is cleared by the glomerulus and can be used to measure glomerular filtration rate (GFR), (Goates et al., 1990). The extraction fraction (the percentage of the agent extracted with each pass through the kidney) of $^{99m}$Tc-DTPA is approximately 20%; for this reason, in patients with impaired renal function this radiopharmaceutical may not be as useful as those with higher extraction efficiencies such as $^{99m}$Tc-mercaptoacetyltriglycine (MAG3) and iodine-131 or iodine-123 orthioiodohippurate (OIH) (Taylor and Nally JV, 1995).

Technetium-99m Methylene Diposphonate ($^{99m}$Tc-MDP) has been clinically used for skeletal imaging for many years. The most common use is a screening test for the detection of bone metastases from malignant tumors. Patients with malignant tumors in the genitourinary tract are likely to have impaired renal function. Renal function has been estimated with $^{99m}$Tc-DTPA. Since these tracers are the same $^{99m}$Tc-labeling agents as $^{99m}$Tc-MDP, patients should undergo both radionuclide studies on different days to estimate renal function and skeletal lesions it is well known that information about the kidneys can be obtained from bone scintigraphy because $^{99m}$Tc-MDP is excreted through the kidneys to provide adequate visualization of the urinary tract. If one can estimate renal function incidental to bone scintigraphy, it is very favorable from the view point of convenience and cost effectiveness. As one quantitative analysis of renal function, measurements of GFR are now performed in clinical practice, particularly with Gate's method (Gates., 1983, Itoh, 2003).

The purpose of the study was to compare the glomerular filtration rate (GFR) obtained by means of a modified Gates' method and $^{99m}$Tc-MDP with those obtained by means of $^{99m}$Tc-DTPA.

In $^{99m}$Tc-DTPA renography, the GFR is calculated without blood or urine sampling (Prigent A, et al., 1999). More recently, calculation of estimated glomerular filtration rate (eGFR) using an empirical mathematical formula has been encouraged as a simple, rapid and reliable means of accessing kidney function (John R., 2004). There are no fewer than 46 different prediction equations currently available although the two most commonly
MATERIAL AND METHODS

Subject Population:
Total of 35 adult patients (23 males, 12 females) were enrolled. Their ages ranged from 18 to 70 years (mean 45± 14). The range of serum creatinine was 0.6-1.4 mg/dl (mean 0.95 ± 0.26 mg/dl, normal 0.6-1.5 mg/dl), and the range of blood urea nitrogen (BUN) was 8.7-32.5 mg/dl (mean 18.7± 5.3mg/dl, normal 8-20mg/dl). All the patients underwent both radionuclide studies with $^{99m}$Tc-MDP and $^{99m}$Tc-DTPA to evaluate bone metastasis and renal function within period of time three weeks. Fifteen patients were diagnosed with hydronephrosis, 13 patients underwent a therapeutic operation.

Renography with $^{99m}$Tc-DTPA:
$^{99m}$Tc-DTPA was prepared according to the manufacturer's instructions with the kits in Radioisotope Laboratories in Nuclear Medicine Department of cesium Unit at Al Kasr Al Aini Hospitals, (Egypt) using a commercially available freeze-dried kits. Counts in pre-injection and post-injection syringes were measured for 60 seconds at 30 cm from the Gamma-Camera (GC901A, Toshiba, Tokyo, Japan), to determine the total amount of activity injected. Prior to the examination, each patient was hydrated with 500-750 ml of water 30 minutes. Renography was carried out with the patient in a supine position with the gamma-camera detector placed under the patient's bed. Rapid injection of 200 MBq of $^{99m}$Tc-DTPA was given through an end welling butterfly needle in an antecubital vein and was followed by infusion of 20 ml of normal saline. A 20% energy window was centered around the 140 keV photo peak. With a 128 x 128 matrix were recorded with an online-computer processing system (GMS-55A, Toshiba), initially at one second per frame for 80 second and then at 20 seconds per frame for 19 minutes.

Renography with $^{99m}$Tc-MDP:
Imaging with $^{99m}$Tc-MDP was performed on another day, for comparison with $^{99m}$Tc-DTPA renography. Data collection and analysis were repeated under the same conditions. Images were comparatively interpreted for kidney size, position, tracer activity, relative to soft tissue and bone uptake, uniformity of tracer distribution, degree of radioisotope retention and pelvicocalyceal dilatation as well as whole body skeleton by two experienced nuclear physicians.

Data Analysis:
Automatically, a region of interest (ROI) was placed around each kidney, and a semilunar background region was placed inferior to each kidney. After background subtraction, time-activity curves (renograms) were generated for both kidneys. With a renogram of each kidney, $T_{\text{max}}$ (time from injection to time of maximum count rate), and $T_{2/3}$ (time from maximum activity above the kidney to time of half twice-maximum count rate) were obtained.

Classification of Renograms:
For comparison, renogram patterns were categorized grossly into the following four patterns fig. (1) Standard pattern (ST), $T_{\text{max}}$ is less than five minutes and renal excretion is prompt, delayed pattern (DY), slow renal excretion regardless of $T_{\text{max}}$, obstructive pattern (OB),$T_{\text{max}}$ occurs at the end of the present time, and hypo functioning pattern (HF), renal washout parallels the cardiac blood pool on the background.

Estimation of Total and Split GFR:
The GFR was determined by a modified Gates' method. Total GFR was obtained with the percent renal uptake of $^{99m}$Tc-DTPA or $^{99m}$Tc-MDP in the ROIs from 2 to 3 minutes after tracer arrival within the kidneys. The following formulas were used according to the manufacturer's software.

\[
\text{Total GFR (ml/min)} = 9.75621 \times (\% \text{ total renal uptake}) - 6.19843 \quad (1)
\]

\[
\% \text{ total renal uptake} = \frac{(L-CNT + R-CNT)}{(\text{reinjection syringe counts-post injection syringe counts})} \times 100 \quad (2)
\]

\[
L-CNT = \frac{(\text{left renal counts} - \text{background counts})/ \exp(-0.153 \times DI)}{361}
\]
R-CNT = \((\text{right renal counts} - \text{background counts})/ \exp (-0.153 \times \text{DI})\)

Where \(L-CNT\) and \(R-CNT\) are the corrected count rates of left and right kidney respectively, kidney depth was estimated from the patient's weight and height by the formulae:

\[
\text{DI (cm)} = 13.3(W/H) + 0.7
\]

Where \(W\) and \(H\) are the patient's weight in kg and height in cm, respectively. The value 0.153 is the linear attenuation coefficient for \(^{99m}\text{Tc}\) radiation in soft tissue. The split GFR was obtained by dividing total GFR by the uptake ratio in 2-3 minutes.

Left split GFR = \(L-CNT/ (L-CNT + R-CNT) \times \text{Total GFR}\)

Right split GFR = \(R-CNT/ (L-CNT + R-CNT) \times \text{Total GFR}\)

**Predicted Creatinine Clearance Methods:**

The GFR was also predicted from the serum creatinine level at renography using Cockcroft-Gault (CG) and Modification of Diet in Renal Disease (MDRD) equations (Akbari A, et al., 2004 and Cockcroft DW, et al., 1978):

- **CG Method:**
  
  **For Men:**
  \[
  \text{GFR (ml/min)} = \{(140-\text{age}) \times \text{weight}\}/(\text{SCr} \times 72)
  \]
  
  **For Women:**
  \[
  \text{GFR (ml/min)} = 0.85 \times \{(140-\text{age}) \times \text{weight}\}/(\text{SCr} \times 72)
  \]
  
  Where weight: body weight (kg), SCr: serum creatinine level (mg/dl).

- **MDRD Method:**
  \[
  \text{GFR (ml/min)} = 186 \times (\text{SCr in mg/dl})^{-1.54} \times (\text{age})^{-0.203}
  \]
  
  for women, multiply with 0.742.

  The GFRs (ml/min) obtained by the previous mentioned four methods was normalized for abody surface area of 1.73m² according to Haycock's equation (Haycock GB et al., 1978).

**Statistical Analysis:**

Data were presented as the means ± SD. Statistical analysis of GFR values obtained with \(^{99m}\text{Tc}\)-MDP versus \(^{99m}\text{Tc}\)-DTPA percent uptake was done by linear regression analysis. The correlation between both tracers was evaluated with Pearson’s correlation coefficient. Statistical significance was defined as \(p < 0.001\).

**RESULTS AND DISCUSSION**

Since MDP is the same \(^{99m}\text{Tc}\)-labeling agent as DTPA, the two examinations should be performed on different days. If one can simultenously estimate renal function and skeletal lesions with \(^{99m}\text{Tc}\)-MDP, it is valuable from the view point of convenience and cost effectiveness. Therefore, the GFR obtained by means of \(^{99m}\text{Tc}\)-MDP were compared with those obtained by means of \(^{99m}\text{Tc}\)-DTPA, and the feasibility of the assessment of renal function with \(^{99m}\text{Tc}\)-MDP was investigated.

**Classification of Renogram Patterns:**

One hundred and forty renograms were obtained on 35 patients using \(^{99m}\text{Tc}\)-DTPAand \(^{99m}\text{Tc}\)-MDP tracers. Of 70 paired renograms, 65 showed the same renogram patterns with both tracers, whereas 5 showed different patterns for the two tracers (fig. 1). Of 5 patients, 3 had hydrenephrosis with different obstructive pattern OB renogram pattern on the \(^{99m}\text{Tc}\)-DTPA renogram versus hydrofunctioning pattern HF or DY pattern on the \(^{99m}\text{Tc}\)-MDP renogram. It was noticed that the count was remarkably less as whole and increase in the count with time was slight, although a \(^{99m}\text{Tc}\)-DTPA renogram showed on OB pattern. Another 2 patients had delayed pattern DY pattern on the \(^{99m}\text{Tc}\)-DTPA renogram versus standard pattern ST pattern on the \(^{99m}\text{Tc}\)-MDP renogram(fig.2).
Estimation of Total GFR and Differential GFR:
The correlation between total and split GFRs obtained by $^{99m}$Tc-DTPA and those obtained by $^{99m}$Tc-MDP are shown in figure 3 and figure 4 (a and b) respectively. Both total and split GFRs obtained by $^{99m}$Tc-DTPA were correlated significantly with those obtained by $^{99m}$Tc-MDP with a correlation coefficient of $r = 0.96 \ (p<0.001)$, $r_{Lt} = 0.973 \ (p<0.001)$ and $r_{Rt} = 0.98 \ (p<0.001)$, respectively.

![Renogram patterns](image)

**Fig. 1:** Renogram patterns. ST: standard pattern, DY: delayed pattern, OB: obstructive pattern, HF: hydrofunctioning pattern.

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**Fig. 2:** Comparison of renogram patterns between the two tracers.

![Correlation between total and split GFR](image)

**Fig. (3):** Correlation between total and split GFR (ml/min) obtained by means of the two tracers.

Estimation of Glomerular Filtration Rate (GFR) predicted by using Cockcroft-Gault's and MDRD equations:
The correlation between GFRs obtained by $^{99m}$Tc-DTPA and those obtained by $^{99m}$Tc-MDP in (ml/min/1.73m$^2$) for 35 adult patients (23 males and 12 females) against the GFRs values that calculated by the CG equation were presented in figures 5 and 6 respectively.
Fig. 4(a): Correlation between differential GFR (ml/min) of left kidney obtained by means of the two tracers.

Fig. 4(b): Correlation between differential GFR (ml/min) of right kidney obtained by means of the two tracers.

Fig. 5: Scatter plot of GFRs (ml/min) obtained by $^{99m}$Tc-DTPA and GFRs calculated by CG equation. The solid line is the regression line showing the correlation between GFRs obtained by two methods.
Fig. 6: Scatter plot of GFRs (ml/min) obtained by $^{99m}$Tc-MDP and GFRs calculated by CG equation. The solid line is the regression line showing the correlation between GFRs obtained by two methods.

Fig. 7: Scatter plot of GFRs (ml/min) obtained by $^{99m}$Tc-DTPA and GFRs calculated by MDRD equation. The solid line is the regression line showing the correlation between GFRs obtained by two methods.

Fig. 8: Scatter plot of GFRs (ml/min) obtained by $^{99m}$Tc-MDP and GFRs calculated by MDRD equation. The solid line is the regression line showing the correlation between GFRs obtained by two methods.
The correlation between GFRs obtained by \(^{99m}\text{Tc-DTPA}\) and those obtained by \(^{99m}\text{Tc-MDP}\) in (ml/min/1.73m\(^2\)) for 35 adult patients (23 males and 12 females) against the GFRs values that calculated by the MDRD equation were presented in figures 7 and 8 respectively.

In evaluation of usefulness of \(^{99m}\text{Tc-MDP}\) for the assessment of renal function there was close correlation between the early (1-3 minutes) renal uptake of \(^{99m}\text{Tc-MDP}\) and \(^{99m}\text{Tc-DTPA}\) (r = 0.96, p<0.001). This is coincident with the data of (Vieras et al., 1991), however, they did not obtain GFR values. Concerning renograms after simultaneous injection of \(^{99m}\text{Tc-MDP}\) and \(^{99m}\text{Tc-DTPA}\), (Jacobson 1995) reported that the peak times would be creditable indicator of renal function because they were the same for both tracers but they also did not obtain the GFR.

Many methods have been proposed to estimate the GFR with \(^{99m}\text{Tc-DTPA}\) (Gates, 1983 and Russel et al., 1985). Of these methods, Gate's method using the gamma camera is the most common which showed that the fractional renal uptake of intravenously administered \(^{99m}\text{Tc-DTPA}\) from 2 to 3 minutes after radiotracer arrival in the kidney was proportional to the GFR. Although this method is easy to use, it is not as accurate as the blood sampling method and contains several technical problems. These problems have included in net injected activity, measurement of kidney depth, background subtraction and attenuation correction (Awdeh et al., 1990 and Taylor, 1999). In comparing the GFR obtained by means of \(^{99m}\text{Tc-MDP}\) and \(^{99m}\text{Tc-DTPA}\), problems with the tracer's energy and attenuation coefficient may be regarded as the same because both tracers are the same \(^{99m}\text{Tc}\)-labeling agents. Because the measurement of kidney depth is important for the estimation of renal function, it is desirable to estimate kidney depth by ultrasonography or the lateral view of scintigraphy in order to minimize errors. The kidney depth was estimated by using the formula for simplicity and consequently, total and deferential GFR were obtained by means of \(^{99m}\text{Tc-MDP}\) correlated well with those obtained by means of \(^{99m}\text{Tc-DTPA}\) (r=0.97, r= 0.98) respectively.

Renographies with \(^{99m}\text{Tc-MDP}\) similar information concerning flow and function to those provided by renographies with provide \(^{99m}\text{Tc-DTPA}\), but the application of \(^{99m}\text{Tc-MDP}\) to renography gives rise to significant problems because this tracer accumulates in the skeleton. However, there have been observed in studies of urinary tract obstruction, post chemotherapy (Lutrin et al., 1994), metastatic calcification (Aktas et al., 2005), renal vein thrombosis (Lamki and Wyatt, 1983), radiation nephritis (Saha GB., 2010), iron overload (Choy et al., 1981), acute tubular necrosis, administration of heparin and nephrotoxic drugs (Bernard et al., 1990), it is certain that the biodistribution of \(^{99m}\text{Tc-MDP}\) can be affected these various conditions. In order to obtain GFR, the percent uptake of 2 to 3 minutes after the radionuclide appearance in the kidneys was used. This gives information regarding renal morphology and renal function incidental to bone scintigraphy with \(^{99m}\text{Tc-MDP}\) (Bostom et al., 2002). If further information is of interest, more definitive renal studies should be performed with \(^{99m}\text{Tc-DTPA}\) (Taylor A, and Eshima D., 1994).

There existed a linear relationship between GFR values that measured by the two tracers against GFR that calculated with CG and MDRD equations.

For CG method the linear regression equation were \(Y = 8.95 + 0.9X\), (r = 0.82, p<0.001) and \(Y=17.052 + 0.75X\) (r = 0.77, p<0.001) respectively.

For MDRD method the linear regression equation were \(13.23 + 3.78X\) (r = 0.78, p<0.001), and \(11.34 + 0.75X\) (r = 0.82, p<0.001) respectively.

The GFRs obtained by \(^{99m}\text{Tc-DTPA}\) and obtained by \(^{99m}\text{Tc-MDP}\) correlated well with those calculated by MDRD and CGequations.

Conclusion:

The assessment of renal function with \(^{99m}\text{Tc-MDP}\) can be performed incidental to bone scintigraphy and is expected to provide useful information in monitoring renal function. The early characteristics of renal handling of \(^{99m}\text{Tc-MDP}\) are sufficiently similar to those of \(^{99m}\text{Tc-DTPA}\) so that, accurate estimation of differential renal function are possible with this agent, and that \(^{99m}\text{Tc-MDP}\) determined renal differential most likely reflects differential glomular filtration rate.

REFERENCES


Bernard, M.S., M. Hayward, C. Hayward and L. Mundy, 1990. Evaluation of intense renal parenchymal...


