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ORIGINAL ARTICLE

Evaluation of the Efficiency of ^{99m}Tc-DMSA as a Radiopharmaceutical in Dynamic Renal Scans

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ABSTRACT

Objective: In dynamic renal scans, ^{99m}Tc-diethylenetriamine pentaacetic acid (DTPA) is copiously used and it yields information about the renal blood-flow and the excretory capacity. ^{99m}Tc-dimercaptosuccinic acid (DMSA) is used for static renal imaging and can likewise uncover the renal cortical structure. This work was intended to evaluate whether DMSA can be declared as a radiopharmaceutical in dynamic renal scans or not. It also aimed at comparing the outcomes procured from DMSA and with DTPA examinations.

Materials and Methods: A comparison of the information gained from the renograms of 47 subjects (normal subjects and subjects with abnormal renal function having: obstructive nephropathy, bilateral nephropathy, hydronephrosis, reduced or non-function kidney, and/or atrophic kidney) who had ^{99m}Tc-DMSA and ^{99m}Tc-DTPA dynamic scintigraphies utilizing the same protocol.

Results: A strong positive correlation had come in view on the evaluation of the left kidney, right kidney, and total glomerular filtration rate (GFR) from ^{99m}Tc-DTPA and ^{99m}Tc-DMSA renograms. In addition, the estimation of the time of the peak height from ^{99m}Tc-DTPA and ^{99m}Tc-DMSA renograms for the right and left kidneys demonstrated as non-significant varieties and a strong positive correlation for both the normal subjects and subjects with kidney abnormalities.

Conclusion: In the light of the outcomes gained from the present investigation, it could be prescribed that ^{99m}Tc-DMSA can favorably replace ^{99m}Tc-DTPA in dynamic renograms in the case of the renal conditions that had been examined in the present work. As scheduled, this will be cost-effective and time saving and will decrease the radiation dose administered to the subjects. Also, the same qualities of results are accomplished with both radiopharmaceuticals in normal subjects and subjects with abnormal renal function.

Keywords: Radiopharmaceutical, GFR, DMSA, DTPA, dynamic renal imaging, static renal imaging.

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INTRODUCTION

Static and dynamic renal scans are the standard scintigraphic techniques for the assessment of renal capacities. These techniques can be proficient in distinct radiopharmaceuticals, e.g., ^{99m}Tc-dimercaptosuccinic acid (^{99m}Tc-DMSA) and ^{99m}Tc-diethylenetriamine pentaacetic acid (^{99m}Tc-DTPA) (1,2). In dynamic renal scintigraphy, ^{99m}Tc-DTPA is used to give information about the renal blood-flow and excretory function. Conversely, ^{99m}Tc-DMSA is used for static renal imaging to visualize the renal cortical structure (3-5). ^{99m}Tc-DMSA was proclaimed to be a magnificent renal imaging agent and was directed to assess the quantitative renal function (6-9). ^{99m}Tc-DMSA can be introduced in the proximal tubular cell either by glomerular filtration and/or direct uptake from the peritubular capillaries as it is largely bound to serum proteins (10-15).

Lee and his partners surveyed the relative renal function in 18 rabbits with unilateral ureteral obstruction in 2010. The relative renal function was figured on ^{99m}Tc-DMSA, ^{99m}Tc-DTPA, or ^{99m}Tc-mercaptoacetyl triglycine (^{99m}Tc-MAG-3) and they uncover that despite the fact there were conflicts between the left and right kidneys, no statistical differences were noted between groups. So, they conclude that dynamic renal imaging agents (^{99m}Tc-DTPA and ^{99m}Tc-MAG-3) can be applied to assess the relative renal function rather than the static image of ^{99m}Tc-DMSA (16). In 2011, Hülya and his co-workers compared relative renal functions (RRFs) acquired from ^{99m}Tc-DTPA and ^{99m}Tc-DMSA in 144 adults with renal diseases. The authors deduced that glomerular rate filtration (GRF) calculated with ^{99m}Tc-DTPA can be used in place of static renal imaging with ^{99m}Tc-DMSA. Additionally, they proclaimed that ^{99m}Tc-DTPA was a suitable method for the evaluation of relative renal function when compared to ^{99m}Tc-DMSA scan. ^{99m}Tc-DTPA can be an alternative for the calculation of relative renal function without a follow-up DMSA scan, particularly in subjects who demand renogram curve and GFR computations (17). In 2011, Zeki and his co-workers concluded that, regarding the calculation of split renal function, ^{99m}Tc-DTPA, ^{99m}Tc-MAG3, and ^{99m}Tc-DMSA renal scans can be reliably employed and each method provides comparable measures (18). In 2012, Demirel and his co-workers determined the differential renal function using DTPA or MAG3 and reported that reliable outcomes were acquired in dynamic renal scan. Also, the functional condition of the kidney could be determined with these protocols. They also proclaimed that MAG3 scintigraphy is a prevalent decision in light of giving preferable data over DTPA about both the capacity of the kidneys and the structure of the renal parenchyma (19).

In 2014, Tanju Çelik and his collaborators inferred that in RRF evaluation, ^{99m}Tc-DTPA was considered as a solid technique similar to ^{99m}Tc-DMSA scan. The authors also reported that ^{99m}Tc-DTPA can be used for the evaluation of relative renal function in subjects who need renogram curve and GFR calculations, whereas ^{99m}Tc-DTPA can be an alternative for the calculation of relative renal function. The authors stated that ^{99m}Tc-DMSA still remains the brilliant standard technique for the calculation of relative renal function (20). Recently, Momin and his partners examined the RRFs estimated with (^{99m}TcDMSA) and (^{99m}TcDTPA) for kidney subjects between 5 months and 71 years. Fifty subjects including 29 males and 21 females have been chosen and applied for renography. The mean RRFs were found to be 52.68%±23.63% and 47.32%±23.63%, respectively, for the left and right kidneys with 99mTc-DMSA measurement. With 99mTc-DTPA, the values were 52.74%±23.54% and 47.26%±23.54% for the same as in DMSA case. The authors found a significant positive correlation (r=0.996, p<0.001) between the RRFs estimated with the two modes. No differences were deduced between the RRFs acquired for the left and right kidneys. The mean difference between the two modes was found to be 0.1. According to the results obtained in their study, both the 99mTc-DMSA and 99mTc-DTPA methods yield similar RRF values. The authors suggested that 99mTc-DMSA is the superior mode for the estimation of RRF, but if the glomerular filtration rate (GFR) and renography were essential, 99mTc-DTPA is the undeniable alternative (21).

The current study was spearheaded on numerous other studies matching the relative renal function calculation results of 99mTc-DMSA and 99mTc-DTPA as there are no past reports (to the best of our knowledge) comparing them as radiopharmaceuticals used in dynamic renal scintigraphies. The former surveys were done in groups of subjects, including adult and pediatric subjects. The present study incorporated a category of normal subjects (either donor or not) undergoing a dynamic renal scan.

The ongoing investigation was outlined to assess whether ^{99m}Tc-DMSA can be incorporated as a dynamic imaging agent and to judge its efficacy as a radiotracer instead of ^{99m}Tc-DTPA in measuring the functionality of the urinary system.

MATERIALS and METHODS

Subjects

This study included 47 subjects (33 males and 14 females) ranging from 14 to 73 years of age; the average age was computed to be 44.515±2.385 and 38.714±3.378 years for males and females, respectively. The 47 subjects were divided into two primary classifications.

Category 1: 18 normal subjects (donor or having routine check) with RRF parameters in the normal range. Category 2: 29 subjects with different renal issues (obstructive nephropathy, bilateral nephropathy, hydronephrosis, reduced or non-function kidney, and/or atrophic kidney). Imaging was done by using two types of radiotracers DTPA and DMSA.

Renography

^{99m}Tc-DTPA was mixed in radioisotope labs in King Fahd Unit, Cairo University Hospitals (Egypt) using a commercially available freeze-dried kit. The dose ranged from 3.5 to 6.5 mCi and was introduced to several subjects with distinct renal diseases in addition to some healthy persons. Before the administration, the pre-injection syringe with a straight needle was checked with two different devices: 1) Dose Calibrator (ATOMLAB 100) and 2) Gamma Camera (Siemens, Orbit, Single head), which was connected to a low-energy general-purpose parallel-hole collimator. The patient was hydrated with 300-500 ml of water, 30 min preceding the examination. The patient laid down on a bed in the supine position, and the image was posteriorly procured. ^{99m}Tc-DTPA was given through a butterfly needle into a vein and was joined by an infusion of 20 ml of normal saline, then 20 mg/2 ml Lasix (Frusemide).

Frames of 128×128 matrices were recorded with an online-computer, initially at 1 s for 1 min and afterward at 10 s for 20 min. The post-injection syringe with a straight needle, which was detached before the injection was again counted by a gamma camera in the same way as a pre-injection. Region of interest (ROI) over each kidney was manually assigned to the frame added from 1 to 3 min following injection. The semilunar background ROI around each kidney was characterized. The background corrected time-activity curve was produced, and the renal uptake of the individual kidney for 1 min after the injection (from 2 to 3 min) was calculated. GFR (GFR Gates) was consequently estimated by a commercially available computer (Oddesey Pegasus Laboratories, Adac) according to the Gates' algorithm.

Standard protocol for the calculation of glomerular filtration rate (GFR)

Peak time (s)

Peak time is defined as the time interval from the beginning of the acquisition to the time when the curve reaches the maximum count.

Half-peak time (s)

Half-peak time (½ peak time) is the time interval from the peak time to the time when the curve reaches half of the maximum counts. For example, if the peak occurs at 400 s and the half-peak occurs at 1600 s, then the half-peak time is 1200 s. Note: A zero value indicates that the application did not find a half-peak time.

Depth (cm)
It is the calculated depth from the body surface to the kidney's center.

Uptake (%)
It is the background–corrected, kidney count take-up from 2 to 3 min after the acquisition was started.

GFR (ml/min)
It is the GFR estimated in ml/min.

Total GFR (ml/min)
Total GFR is the summation of the GFR for both the right and left kidneys.

Normalized GFR (ml/min)
Normalized GFR to the body surface area was calculated by dividing 1.73 m^2 by the body surface area. It is estimated based on the patient's height and weight, and later, the result is multiplied by the GFR.

GFR (ml/min)=(%renal uptake×9.8127)−6.82519 (Equation 1)

Where 9.8127 is the regression coefficient (R) and −6.82519 is the y-intercept (22).

The percent renal uptake in Equation 1 is calculated according to the method reported by Gates (1984) as follows:

(Equation 2) (23)

Where, Rt Kidney cts: right kidney counts, bkg: background counts, Lt Kidney cts: left kidney counts, Pre-& Postinj. cts: pre-& post-injection counts, µ: linear attenuation coefficient of ^{99m}Tc in soft tissue (24), which is equal to 0.153 and x: kidney depth in centimeters.

From Equation 2, it is clear that that the the percent uptake of the left kidney plus the percent uptake of the right kidney, at 2-3 min, post-injection is calculated by dividing the background and depth-corrected kidney counts by the total net counts injected and multiplying the result by 100. The normalized and depth-corrected kidney counts and the total net counts are obtained from the nuclear medicine renogram study.

The total net counts injected are determined by the pre- and post-injection syringe images. The post-injection counts are then corrected for decay to compensate for "excess time" between the pre- and post-injection images. Ultimately, the decay-corrected, post-injection syringe counts are taken off from the pre-injection syringe counts to yield the total net counts injected. The normalized and corrected kidney counts are determined from 60 s of data collected 2-3 min following the tracer positioned in the kidney. To obtain an accurate sampling of the renal uptake, a dynamic study in a 128×128 matrices is acquired at 10-15 s/frame for 6 transactions, immediately after the administration of the tracer. A composite image is built from the dynamic study. Areas of interest are formed for each kidney and in the corresponding background areas. The background areas are then normalized to their respective renal areas, and the counts in the normalized background areas are subtracted from the counts in the renal areas to obtain the normalized net kidney counts. After that, the same steps were iterated with DMSA radiotracer.

Figure 1 shows an image of a patient's dynamic DMSA scan using the same protocol as in DTPA renal scans.

Statistical Analysis
Data analysis was carried out using Origin software version 6.

RESULTS

Imaging was done by using two types of radiotracers DTPA and DMSA.

Table 1. The mean±standard deviation and p-values of relative renal function calculated for each category

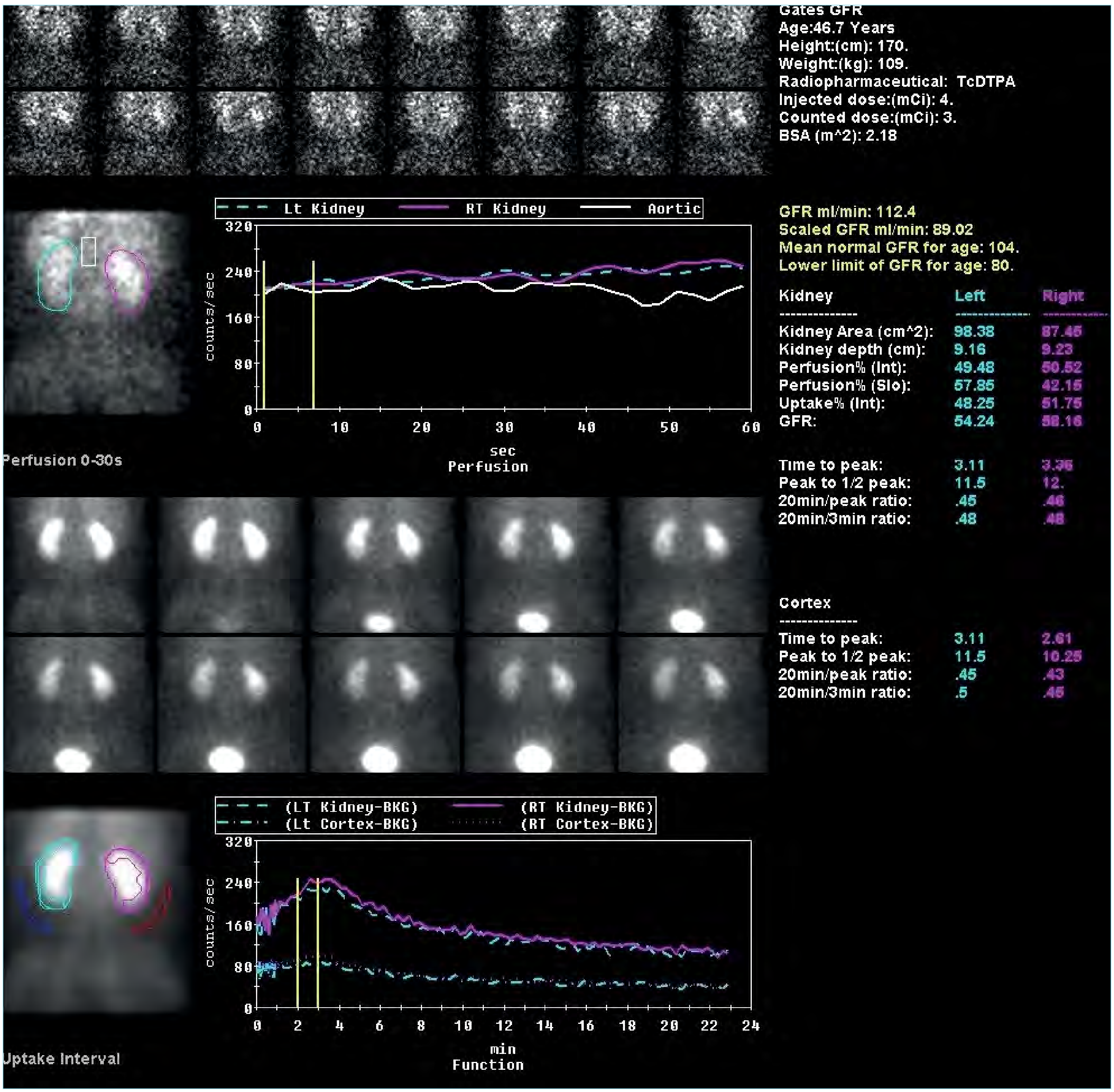
		Category 1			Category 2		
		Mean Value	Standard Deviation	p	Mean Value	Standard Deviation	p
DMSA	Mean Left Kidney GFR	36.80%	3.2	0.64	30.31%	4.70	0.72
	Mean Right Kidney GFR	46.11%	2.12	0.86	27.45%	4.44	0.91
	Total GFR	94.01%	2.98	0.60	57.57%	4.38	0.61
	Time To The Peak Height Left Kidney	4.23%	0.87	0.85	8.56%	1.23	0.99
	Time To The Peak Height Right Kidney	4.07%	0.83	0.91	5.73%	1.73	0.88
DTPA	Mean Left Kidney GFR	38.83%	3.26	0.64	32.75%	4.96	0.72
	Mean Right Kidney GFR	46.67%	2.27	0.86	28.16%	4.36	0.91
	Total GFR	96.17%	2.80	0.60	60.80%	4.44	0.61
	Time To The Peak Height Left Kidney	4.23%	0.88	0.85	8.53%	1.37	0.99
	Time To The Peak Height Right Kidney	3.80%	0.83	0.91	5.97%	1.19	0.88

DMSA: ^{99m}Tc-dimercaptosuccinic acid; DTPA: ^{99m}Tc-diethylenetriamine pentaacetic acid; GFR: glomerular filtration rate

Table 2. The correlation analysis values from 99mTc-DTPA and 99mTc-DMSA renograms calculated for each category

Correlation Analysis From ^{99m}Tc-DTPA And ^{99m}Tc-DMSA Renograms	R Value For Category 1	R Value For Category 2	At A Significance Level Of 0.05
Left Kidney GFR	0.96	0.99	Strong Positive Correlation
Right Kidney GFR	0.91	0.98	Strong Positive Correlation
Total GFR	0.88	0.96	Strong Positive Correlation
Time To The Peak Height Left Kidney	0.97	0.89	Strong Positive Correlation
Time To The Peak Height Right Kidney	0.95	0.92	Strong Positive Correlation

DMSA: ^{99m}Tc-dimercaptosuccinic acid; DTPA: ^{99m}Tc-diethylenetriamine pentaacetic acid; GFR: glomerular filtration rate; R: correlation coefficient



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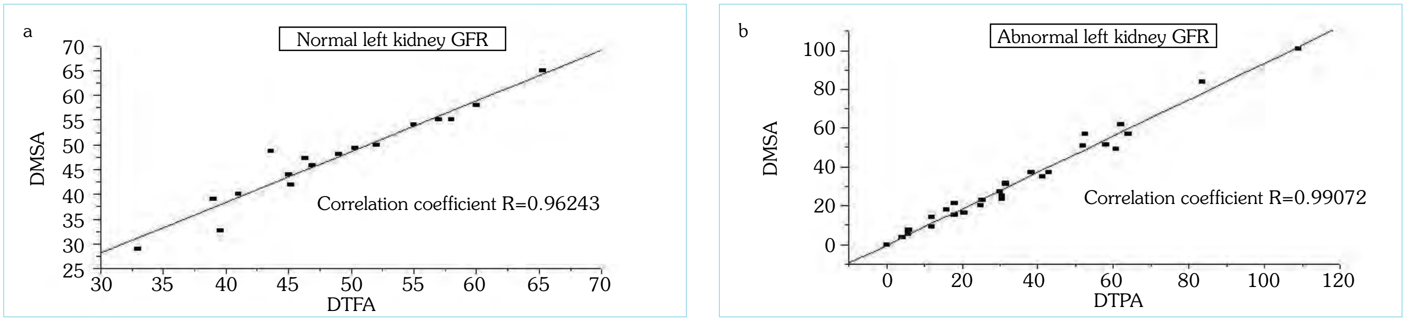

Figure 2. a, b. **(a) Correlation between the left kidney GFR as measured from 99mTc-DTPA and 99mTc-DMSA renograms for category 1 (normal subjects). (b) Correlation between the left kidney GFR as measured from 99mTc-DTPA and 99mTc-DMSA renograms for category 2 (subjects with abnormal renal functions).**

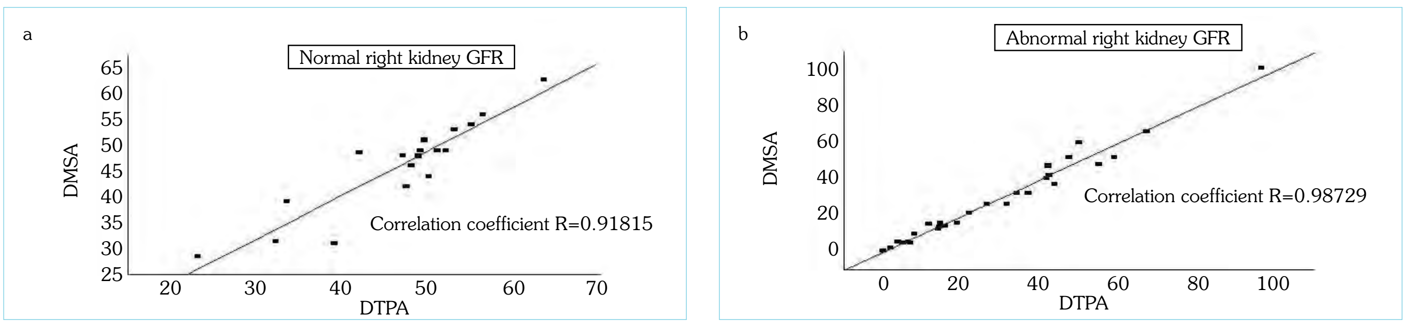

Figure 3. a, b. **(a) Correlation between the right kidney GFR as measured from 99mTc-DTPA and 99mTc-DMSA renograms for category 1 (normal subjects). (b) Correlation between the right kidney GFR as measured from 99mTc-DTPA and 99mTc-DMSA renograms for category 2 (subjects with abnormal renal functions).**

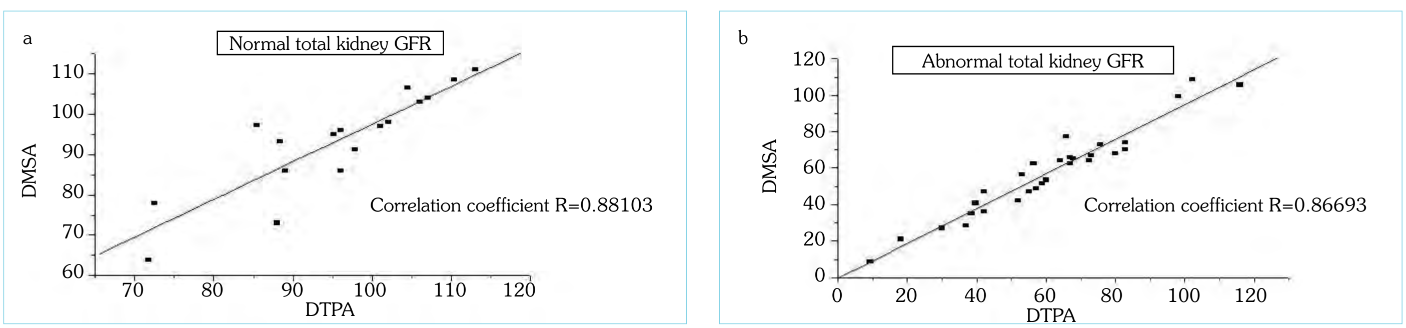

Figure 4. a, b. **(a) Correlation between the total GFR as measured from 99mTc-DTPA and 99mTc-DMSA renograms for category 1 (normal subjects). (b) Correlation between the total GFR as measured from 99mTc-DTPA and 99mTc-DMSA renograms for category 2 (subjects with abnormal renal functions).**

GFR was computed for each category with both radiopharmaceuticals DMSA and DTPA. Estimating the mean±standard deviation and P-values (the left and right kidney GFR, the average total kidney GFR, and the time to the peak height from both kidneys) for category 1 (normal subjects) and category 2 (subjects with abnormal renal functions) depicted no statistical significance according to the 99mTc-DTPA and 99mTc-DMSA renograms at a significance level of 0.05 as seen in Table 1. In correlation analysis for the previously mentioned calculations, the analysis showed a strong positive correlation between 99mTc-DMSA and 99mTc-DTPA for both categories 1 and 2 as seen in Table 2.

The correlation analysis for the left and right kidney GFR, the total kidney GFR, the time to the peak height recorded from the left kidney, and the peak height from the right kidney showed a strong positive correlation between 99mTc-DMSA and 99mTc-DTPA for both categories 1 and 2 ($r1=0.96$ and $r2=0.99$; $r1=0.91$ and $r2=0.98$; $r1=0.88$ and $r2=0.96$; $r1=0.97$ and $r2=0.89$; and $r1=0.95$ and $r2=0.92$, respectively) as seen in (Figure 2 a and b, Figure 3 a and b, Figure 4 a and b, Figure 5 a and b and Figure 6 a and b, respectively).

DISCUSSION

The present work was based on many other studies matching the relative renal function computation results of 99mTc-DMSA and 99mTc-DTPA. However, to our knowledge, there are no reports handling them as a radiopharmaceutical used in dynamic renal scintigraphy using the same protocol used with 99mTc-DTPA in dynamic renal scan. In the literature, there are many reports comparing relative renal function estimated with 99mTc-DTPA and 99mTc-DMSA in adults and children. Nevertheless, in that respect, there is no consensus about the results. In some articles, it is emphasized

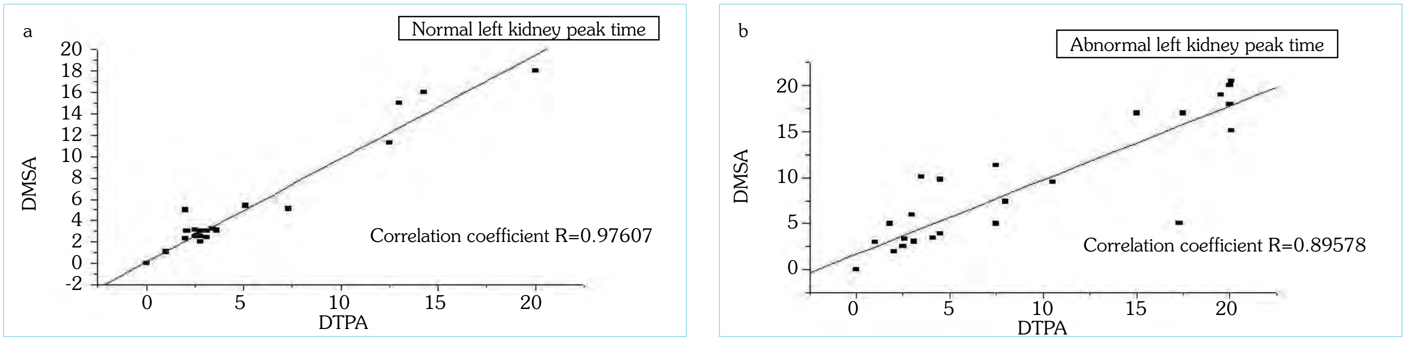

Figure 5. a, b. Correlation between the time to the peak height for the left kidney as measured from ^{99m}Tc-DTPA and ^{99m}Tc-DMSA renograms for category 1 (normal subjects). (b) Correlation between the time to the peak height for the left kidney as measured from ^{99m}Tc-DTPA and ^{99m}Tc-DMSA renograms for category 2 (subjects with abnormal renal functions).

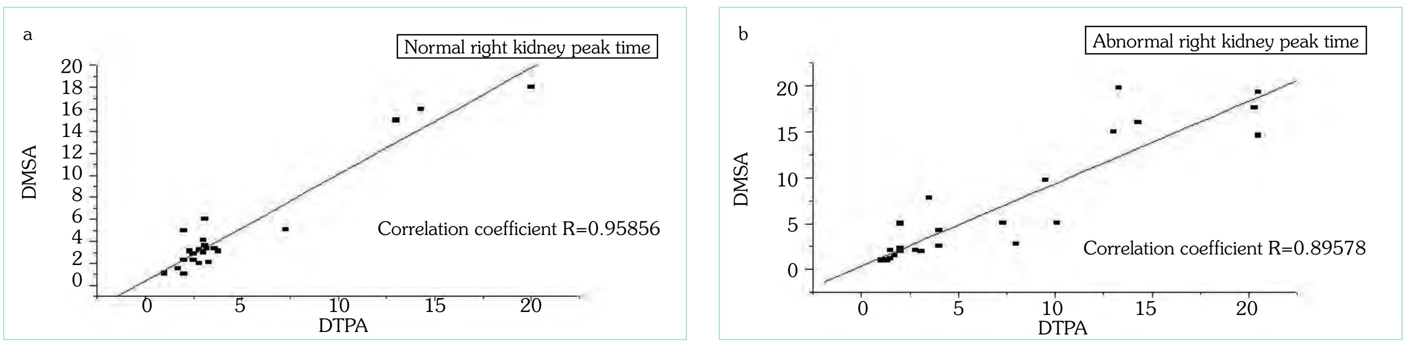

Figure 6. a, b. Correlation between the time to the peak height for the right kidney as measured from ^{99m}Tc-DTPA and ^{99m}Tc-DMSA renograms for category 1 (normal subjects). (b) Correlation between the time to the peak height for the right kidney as measured from ^{99m}Tc-DTPA and ^{99m}Tc-DMSA renograms for category 2 (subjects with abnormal renal functions).

that relative renal function calculated with ^{99m}Tc-DTPA is as reliable as ^{99m}Tc-DMSA (18). Conversely, in some of the works, it is declared that ^{99m}Tc-DTPA is not as good as ^{99m}Tc-DMSA in relative renal function calculation (1, 11). Data analysis for the present study revealed non-significant changes between the left and right kidney GFR, total kidney GFR, time to the peak height of the right and left kidneys in the study categories (normal subjects and abnormal renal function subjects) with both tested radiopharmaceuticals ^{99m}Tc-DTPA and ^{99m}Tc-DMSA during dynamic renal scans. From the current study results, it is obvious that 99mTc-DTPA and 99mTc-DMSA radiotracers can be substituted by each other without any impingement on the quality of the effects obtained during dynamic renograms. One interesting finding obtained from the current study is that using ^{99m}Tc-DMSA in dynamic renal scintigraphy is more favorable in cases of subjects with abnormal renal function (category 2) than in normal cases (as drawn from the higher values of the correlation coefficient calculated for all the previously mentioned renogram parameters). However, there are some differences between DTPA and DMSA. These variations are due to discrete biological characteristics of the two radiopharmaceuticals, such as methods of renal excretion, renal cell retention of radioactive material, the degree of plasma-protein bound, and degree of plasma clearance. ^{99m}Tc-DMSA is taken up in the proximal tubular cells and also in the upper part of the loop of Henle (24). It has been reported that ^{99m}Tc-DMSA-protein binding is approximately 90% (16,28), the author deduced deduced that DMSA is fixed into the cortical cell whereas the rest of DMSA is filtered at the glomerulus. On the other hand, 99mTc-DTPA is cleared by the glomerulus (>95%) and a small fraction may be bound to the protein (29). These variations in filtration through glomerulus clearly appear in normal subjects. For this reason, the values of the correlation coefficient between DTPA and DMSA in category 2 (subjects with renal abnormalities) are stronger and more positive than in category 1 (normal subjects), especially in case of total GFR for both kidneys ($r2>r1=0.96>0.88$).

Although in the study of Domingues and co-workers (2006), in which they estimated the RRFs with ^{99m}Tc-DTPA and ^{99m}Tc-EC were compared with the results of ^{99m}Tc-DMSA. The authors deduced that the relative renal function estimated with technetium-^{99m} ethylenedicysteine (^{99m}Tc-EC) was corresponding to ^{99m}Tc-DMSA results, but the results of relative renal function calculated with ^{99m}Tc-DTPA were statistically distinct, which disagree with our results (1).

Our study has some limitations within which our finding needs to be carefully interpreted. Foremost, the range of age tested was large, which may affect the results, as GFR levels vary according to the age. We too recommend categorizing the "subjects with abnormal kidney function" into further groups according to their diagnosis and re-perform the analysis to decide which is the best condition, wherein 99mTc-DMSA is as reliable as 99mTc-DTPA. Finally, there is a considerable external clearance by the liver and spleen, which if taken into consideration would give more accurate results.

CONCLUSION

Although ^{99m}Tc-DTPA is currently the most reliable radiotracer used in dynamical renal imaging, in the light of the cases of renal diseases studied in the present work (non-function right kidney, advanced nephropathy of the right kidney, nephropathy of the right kidney, reduced right kidney function, left hydronephrosis, left kidney stone, bilateral hydronephrosis, and left loin pain), it may be suggested that ^{99m}Tc-DMSA can be successfully considered as a replacer for ^{99m}Tc-DTPA in dynamic renogram with the same quality of results, which will have the following avails: as ^{99m}Tc-DMSA is the most reliable mechanism for the calculation of relative renal function and, in our case, replacing ^{99m}Tc-DTPA with ^{99m}Tc-DMSA as a radiopharmaceutical in dynamic renogram, this will give the chance for using only ^{99m}Tc-DMSA for both types of renograms, which will be time and money-sparing as ^{99m}Tc-DMSA is an economical and easy method to be acquired (30). Moreover, this will decrease the effort of the physicist in preparing the radiopharmaceutical material and will also decrease suffering by lowering the dose taken by subjects.

Ethics Committee Approval: Patient's anonymity was carefully protected and any experimental investigation with human subjects was following the guidelines required by the institution.

Informed Consent: Written inform consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Conceived and designed the experiments or case: HMY. Performed the experiments or case: IMM, SEM, SSH. Analyzed the data: IMM. Wrote the paper: HMY, IMM, SEM, SSH. All authors have read and approved the final manuscript.

Conflict of Interest: The authors have no conflict of interest to declare.

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