Evaluation of ^{99m}Tc- MAG3/DTPA Radiopharmaceuticals in Detection of Hydronephrosis

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Abstract: The aims of this study were to evaluate the use of quantitative T½ values in the detection of obstructive and non-obstructive hydronephrosis using the radiopharmaceuticals 99mTc-MAG3 and 99mTc-DTPA, to define the T½ ranges of each type of hydronephrosis (HyN) in Sudan, and to determine the radiopharmaceutical of choice for the detection of HyN.
Between January 2009 and November 2009, 100 patients suffering from HyN were divided into two groups at two different hospitals (RICK, ELNILINE), and each group of 50 patients was injected with a different radiopharmaceutical (group 1 with 99mTc-MAG3 at RICK and group 2 with 99mTc-DTPA at ELNILINE). Standardized diuretic renograms were obtained in nuclear medicine centers. T½ readings in the range of 0–8 min were regarded to indicate a Non-Ob/HyN kidney. Normal T½ readings in the range of >8 to 12 min also revealed that in patients in group 1 (99mTc-MAG3 at RICK) who had Ob/HyN and had T½ readings greater than 12 min, HyN was affecting the right kidney more than the left kidney. Drainage half-time clearances (T½) were lower in all cases of HyN injected with 99mTc-MAG3 compared to cases injected with 99mTc-DTPA, which makes it the radiopharmaceutical of choice for the detection of HyN. This study concluded that 99mTc-MAG3 showed lower T½ readings in comparison to 99mTc-DTPA, which indicates that 99mTc-MAG3 is cleared faster than 99mTc-DTPA in all pathological conditions of hydronephrosis (non-obstructive and obstructive HyN).
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1. Introduction

The use of radioisotopes in studies of the urinary system is dedicated to achieving three major goals: quantification of renal function; and dynamic imaging, i.e., renography and parenchymal scintigraphy (Leuven ,2006).

The use of technetium-99m mercaptoacetyltriglycine (MAG3) has increased significantly since its introduction in 1986 (Fritzberg et al. 1986, Taylor et al. 1986).

Because of the favorable imaging characteristics of 99mTc and the more efficient renal extraction of 99mTc-MAG3 compared to 99mTc iethylenetriaminepentaacetic acid (DTPA), 99mTc MAG3 has become the radiopharmaceutical of choice in many clinical contexts, particularly for patients with suspected obstruction and/or impaired renal function (O'Reilly et al. 1996.,Taylor et al 1994.,Gordon et al.2001,IMV Medical information division. 2003Because of the favorable imaging characteristics of 99mTc and the more efficient renal extraction of 99mTc-MAG3 compared to 99mTc diethylenetriaminepentaacetic acid (DTPA), 99mTc MAG3 has become the radiopharmaceutical of choice in many clinical contexts, particularly for patients with suspected obstruction and/or impaired renal function (O'Reilly et al. 1996, Taylor et al. 1994, Gordon et al. 2001, IMV Medical Information Division 2003).).

At present, ^{99m}Tc-MAG3 is estimated to account for approximately 70% of the 590,000 renal scans performed annually in the United States, but many renal scans are interpreted by diagnosticians at sites that perform less than three studies per week (Schlegel et al. 1976).

Clearance measurements and other specific quantitative parameters have been recommended to assist in scan interpretation and patient management (Gates et al. 1982, Russell et al. 1996, Bubeck et al. 1993, Blaufox et al. 1996, Müller-Suur et al. 1998, Taylor et al. 1996).

For example, to assist in the interpretation of angiotensin converting enzyme inhibition renography, the Santa Fe consensus report and the Society of Nuclear Medicine procedure guideline on renovascular hypertension recommend measurements of time to maximum counts (Tmax) and 20 min/maximum count ratios for whole kidney and cortical regions of interest (Taylor et al. 2003, Russell et al 1994).

The 20 min/2–3 minute count ratio has been proposed as a useful parameter to simultaneously evaluate clearance and excretion and may be especially useful in monitoring transplant patients to distinguish between acute tubular necrosis and rejection (Piepsz et al. 2000).

A measurement of urine drainage based on a quantitative comparison of post-void kidney counts to counts obtained during the pre-void period improves the sensitivity and specificity of detecting an obstructed kidney (Gordon et al. 1988, Wong et al. 2000).

This study was conducted to evaluate the time to half-maximum activity (T½) values of common radiopharmaceuticals (^{99m}Tc-DTPA and ^{99m}Tc-MAG3) in the detection of hydronephrosis in Sudan.

2.Material and methods

Subjects

This study was conducted in the nuclear medicine department at Khartoum Radioisotopes Center in the period between January 2009 and November 2009. One hundred patients suspected of hydronephrotic kidneys were included in this study. All patients were referred for an assessment of renal outflow obstruction and function. They were divided into two groups: group one, 50 patients with hydronephrosis that underwent a ^{99m}Tc-MAG3 nuclear medicine study at RICK Hospital, while group two consisted of the other 50 patients with hydronephrosis who underwent a ^{99m}Tc-DTPA nuclear medicine study at Elnilen Hospital.

Methods

Renography with ^{99m}Tc-DTPA

^{99m}Tc-DTPA was administered at a dose of 10–15 mCi or 370–555 MBq. Prior to imaging, the patient was well-hydrated with 500 mL of water; children were hydrated orally at 15 mL/kg prior to scanning or at 10 mL/kg with a general formula IV. If possible, the patient was made to lie in a supine position with the camera's face centered at the umbilical region. The patient was asked to remain at rest with no motion. If this was not possible (e.g., with children), then further measures were taken, such as providing the patient with a short-acting sedative.

The computer capturing the start of ^{99m}Tc-DTPA administration was set up to acquire 5-s frames for approximately 5 min. At least 30 s of data were acquired before the child was given the signal to void to allow establishment, usually for the first flow (angiogram). The computer was set for 2–3 s / frame × 1 min; however, for dynamic studies, it was set for 15–30 s / frame × 20–30 min.

Renography with ^{99m}Tc-MAG3

All patients underwent routine ^{99m}Tc-MAG3 diuretic renography using a standardized protocol, and bladder catheterization was not performed. All patients were hydrated with 300–500 mL of oral fluids 30 min before the injection of ^{99m}Tc-MAG3. Furosemide 1 mg/kg was intravenously administered 20 min before the injection of the ^{99m}Tc-MAG3 radiopharmaceutical (F + 20 protocol). We administered approximately 1.85 MBq/kg (50 µCi/kg) ^{99m}Tc-MAG3 or a minimum dosage of 37 MBq (1 mCi) intravenously.

The dynamic study was set as 2 s / frame for the first minute followed by 1 min / frame for 20 min. For the measurement of differential renal function and renogram generation, regions of interest were drawn over the entire kidney and background on each side.

Data were analyzed using SPSS software. Informed consent was obtained from all patients included in the study. The mean, standard deviation, and range are used to describe normal values.

3. Results

T½ values were calculated from the time demonstrating the maximum number of counts to the time when the renogram curves decreased to half of the maximum counts. Based on a study reported by Mettler et al. (2006), patients who participated were categorized into three groups using the whole kidney as a region of interest (ROI): (a) non-obstructive hydronephrosis; (b) normal; and (c) obstructive hydronephrosis.

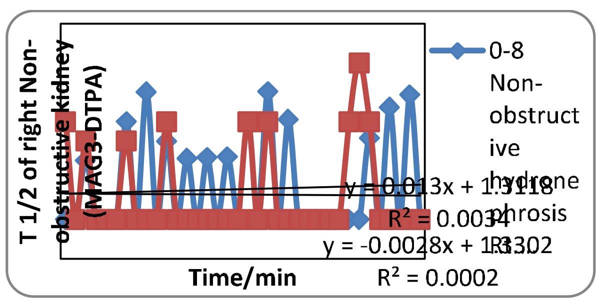

Figure 1: shows graphical representation of comparison between R.t kidneys for patients in sample whom been injected either by ^{99m}Tc-MAG and ^{99m}Tc-DTPA in time interval between (0-8min) which represents (non-obstructive hydronephrosis) cases in the sample.

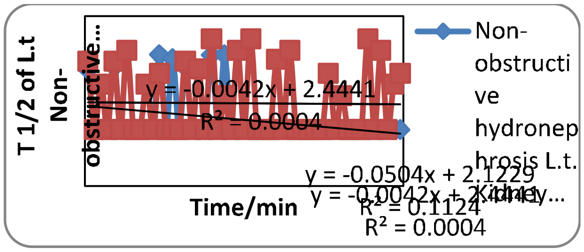

Figure 2: shows graphical representation of comparison between L.t kidneys for patients in sample whom been injected either by 99mTc-MAG and 99mTc-DTPA in time interval between (0-8min) which represents (non-obstructive hydronephrosis) cases in the sample.

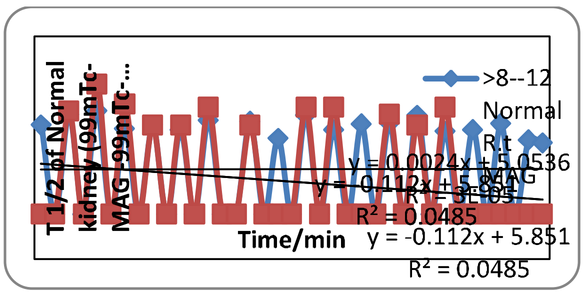

Figure 3: shows graphical representation of comparison between R.t kidneys for patients in sample whom been injected either by 99mTc-MAG and 99mTc-DTPA in time interval between (<8-12min) which represents (Normal R.t kidneys) cases in the sample.

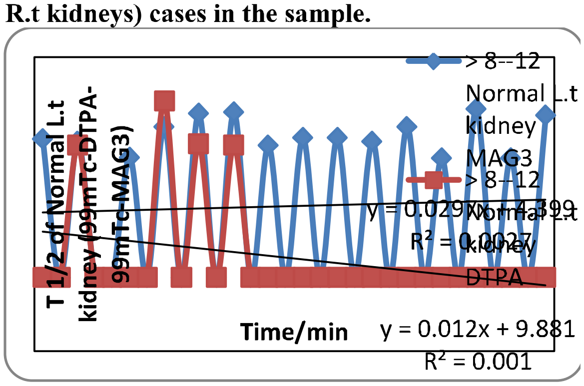

Figure 4: shows graphical representation of comparison between L.t kidneys for patients in sample whom been injected either by 99mTc-MAG and 99mTc-DTPA in time interval between (< 8-12min) which represents (Normal L.t kidneys) cases in the sample.

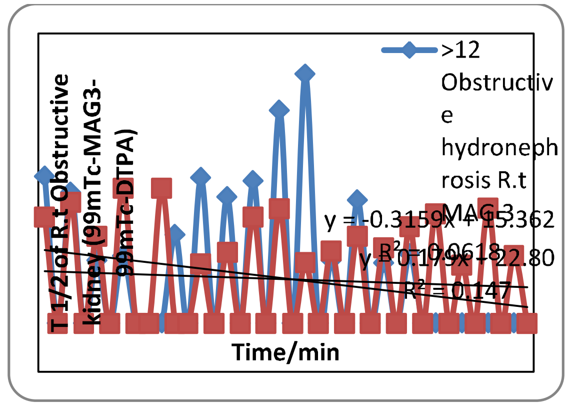

Figure 5: shows graphical representation of comparison between R.t kidneys for patients in sample whom been injected either by 99mTc-MAG and 99mTc-DTPA in time interval between (<12 min) which represents (obstructive hydronephrosis) cases in the sample.

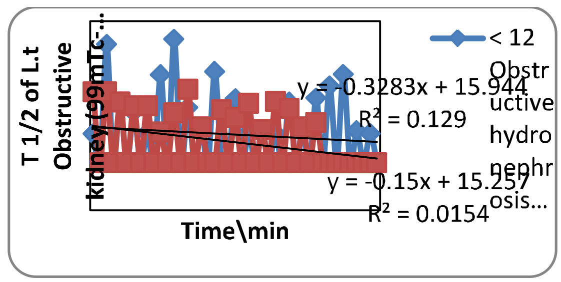

Figure 6: shows graphical representation of comparison between L.t kidneys for patients in sample whom been injected either by 99mTc-MAG and 99mTc-DTPA in time interval between (<12 min) which represents (obstructive hydronephrosis) cases in the sample.

4. Discussions

Figure 1 shows comparison between T ½ readings of R.t. kidney in time interval (0-8) which represents Non-Obstructive hydronephrotic kidneys in both groups (1(99mTc-MAG3),2(99mTc-DTPA)), Such comparison reveal that the relationship between the elapsed time of radiopharmaceutical and T ½ readings for patients injected with99mTc-MAG3 as follows: $y = 0.056x + 3.633$, and for patients injected with 99mTc-DTPA as follows: $y = 0.056x + 4.156$, where x refer to elapsed time and y refer to T ½ reading for the Rt.kidney with Non-Ob\HyN in both equations, from these equations we conclude that 99mTc-MAG3 is released more rapidly from kidney than 99mTc-DTPA, the reason to the differentiation of extraction efficiency for the radiopharmaceuticals (99mTc-MAG3, 99mTc-

DTPA) because Non-obstructive hydronephrotic kidney is usually result from infection, vesicouretral reflux, or previous obstruction, this will increase the pelvic pressure inside the kidney, and as 99mTc-MAG3's extraction efficiency is 95% mainly through tubuler secretion and 99mTc-DTPA's extraction efficiency is 20% mainly through glumeuler filtration, the above causes of Non-Obstructive hydronephrosis will directly increase the tubuler rejection back to collecting tubules, which is in turn will reduce the T ½ value of 99mTc-DTPA, This result shows agreement with previous studies (François et al **(**1992**)**. Adil et al (1988). Figure 1 shows a comparison between the T½ readings in the right kidneys in the time interval from 0 to 8 min, which represents non-obstructive hydronephrotic kidneys in both groups (group 1, ^{99m}Tc-MAG3; group 2, ^{99m}Tc-DTPA). Such comparisons revealed that the relationship between the elapsed time of the radiopharmaceutical and T½ readings for patients injected with ^{99m}Tc-MAG3 can be described as follows: $y = 0.056x + 3.633$; and for patients injected with ^{99m}Tc-DTPA, the relationship was as follows: $y = 0.056x + 4.156$, where x refers to the elapsed time and y refers to the T½ reading for the right kidney with Non-Ob/HyN in both equations. From these equations, we conclude that ^{99m}Tc-MAG3 is released more rapidly from the kidney than ^{99m}Tc-DTPA, because of the different extraction efficiencies of the radiopharmaceuticals ^{99m}Tc-MAG3 and ^{99m}Tc-DTPA. Because a non-obstructive hydronephrotic kidney usually results from infection, vesicoureteral reflux, or previous obstruction, this will increase the pelvic pressure inside the kidney. As the extraction efficiency of ^{99m}Tc-MAG3 is 95%, mainly through tubular secretion, while the extraction efficiency of ^{99m}Tc-DTPA is 20%, mainly through glomerular filtration, the above causes of non-obstructive hydronephrosis will directly increase tubular rejection back into the collecting tubules, which in turn reduces the T½ value of ^{99m}Tc-DTPA. This result is in agreement with the results of previous studies (Jamar et al. 1992, Al-Nahhas et al. 1988).

Figure 2 shows a comparison between the T½ readings of the left kidneys in the time interval from 0–8 min, which represents non-obstructive hydronephrotic kidneys in both groups (group 1, ^{99m}Tc-MAG3; group 2, ^{99m}Tc-DTPA). Such comparisons revealed that the relationship between the elapsed time of the radiopharmaceutical and the T½ readings of patients injected with ^{99m}Tc-MAG3 can be described as follows: $y = 0.057x + 5.304$; and for patients injected with ^{99m}Tc-DTPA, as follows: $y = 0.002x + 5.676$, where x refers to the elapsed time and y refers to the T½ values for left kidneys with Non-Ob/HyN in both equations. From these equations, we conclude that ^{99m}Tc-MAG3 is released more rapidly from the kidney than ^{99m}Tc-DTPA. The research suggests the reason is related to the difference in extraction efficiency between the radiopharmaceuticals ^{99m}Tc-MAG3 and ^{99m}Tc-DTPA. Because non-obstructive hydronephrotic kidney usually results from infection, vesicoureteral reflux, or previous obstruction, this increases the pelvic pressure inside the kidney. As the extraction efficiency of ^{99m}Tc-MAG3 is 95%, mainly through tubular secretions, and the extraction efficiency of ^{99m}Tc-DTPA is 20%, mainly through glomerular filtration, the above causes of non-obstructive hydronephrosis will directly increase tubular rejection back into the collecting tubules, which in turn will reduce the T½ values of ^{99m}Tc-DTPA. This result is also in agreement with previous studies.

Figure 3 shows a comparison between T½ readings of the right kidneys during the time interval from 8 to 12 min, which represents normal kidney readings in both groups (group 1, ^{99m}Tc-MAG3; group 2, ^{99m}Tc-DTPA). These graphs reveal that patients from both groups who are truly diagnosed with normal kidneys fell in the range of 8–12 min. This result is in agreement with previous studies (Jamar et al. 1992, Al-Nahhas et al. 1988).

This result also provides a statistical comparison between the two radiopharmaceuticals by means of T½ readings during normal kidney status, where it was revealed that ^{99m}Tc-MAG3 was excreted more rapidly from the kidney than ^{99m}Tc-DTPA. According to the following equations, the relationship between the elapsed time of the radiopharmaceutical and the T½ readings for patients injected with ^{99m}Tc-MAG3 was as follows: $y = -0.040x + 10.73$; for ^{99m}Tc-DTPA, the equation was: $y = -0.038x + 12.08$. This may result from the fact that ^{99m}Tc-MAG3 has an extraction efficiency twice that of ^{99m}Tc-DTPA, whereas ^{99m}Tc-MAG3 is concentrated in the kidney (which produces more satisfactory images) through two pathways: tubular secretion, 90–95% and glomerular filtration, 5–10%, while ^{99m}Tc-DTPA is approximately 20% (extraction fraction) bound to plasma protein. Tubular secretion renal agents are preferred because they result in lower radiation exposure to the patient (rapid excretion) and provide satisfactory images through higher extraction efficiency and good biodistribution in the renal parenchyma, showing agreement with previous studies (Mettler et al. 2006, Adachi et al. 1994, Inoue et al. 1999, Karam et al. 2009)

Figure 4 shows comparisons between T½ readings of the left kidneys during the time interval from >8 to 12 min, which represents normal kidney readings in both groups (group 1, ^{99m}Tc-MAG3; group 2, ^{99m}Tc-DTPA). Such graphs reveal that patients from both groups 1 and 2 who were truly diagnosed with normal kidneys fell in the range of >8 to 12 min. This result is in agreement with the results of previous studies (Jamar et al. 1992, Al-Nahhas et al. 1988).

This result also provides a statistical comparison between the two radiopharmaceuticals by means of T½ readings during normal kidney status, where it was revealed that ^{99m}Tc-MAG3 is excreted more rapidly from the kidney than ^{99m}Tc-DTPA. According to the following equations, the relationship between the elapsed time of the radiopharmaceutical and the T½ readings for patients injected with ^{99m}Tc-MAG3 was as follows: $y = 0.011x + 9.539$; for ^{99m}Tc-DTPA, the equation was $y = 0.012x + 9.881$. This may result from the fact that ^{99m}Tc-MAG3 has an extraction efficiency twice that of ^{99m}Tc-DTPA, whereas ^{99m}Tc-MAG3 is concentrated in the kidney (which produces more satisfactory images) through two pathways: tubular secretion, 90–95%, and glomerular filtration, 5–10%, while ^{99m}Tc-DTPA is approximately 20% (extraction fraction) bound to plasma protein. Tubular secretion renal agents are preferred because they result in lower radiation exposure to the patient (rapid excretion) and provide satisfactory images through higher extraction efficiency and good biodistribution in the renal parenchyma, showing agreement with previous studies (Mettler et al. 2006, Adachi et al. 1994, Inoue et al. 1999). Figure 5 shows comparisons between T½ readings of the kidney during the time interval >12 min, which represents obstructive hydronephrosis cases in both groups (group 1, ^{99m}Tc-MAG3; group 2, ^{99m}Tc-DTPA). Such graphs reveal that patients from both groups 1 and 2 who were truly diagnosed with obstructive HyN fell in the range of >12 min; this result is in agreement with previous studies (The relationship between the elapsed time of the radiopharmaceutical and the T½ readings for patients injected with ^{99m}Tc-MAG3 was as follows: $y = 0.018x + 25.26$; for ^{99m}Tc-DTPA, the equation was $y = -0.179x + 22.80$, which reveals that ^{99m}Tc-MAG3 is also released more rapidly from the kidney than ^{99m}Tc-DTPA, and the research has revealed that this occurs because of two reasons. The first reason is that ^{99m}Tc-MAG3 has a higher extraction efficiency than ^{99m}Tc-DTPA, and the second reason is that ^{99m}Tc-MAG3 has a better response to furosemide (which is injected 15–20 min after the administration of the radiopharmaceutical). Furosemide is a strong diuretic compound to help the obstructed kidney wash the radiopharmaceutical into the urinary bladder. These results showed agreement with previous studies (Karam et al. 2009, Taylor et al. 1994).

Figure 6 shows comparisons between T½ readings of the left kidneys in the time interval >12 min, which represents obstructive hydronephrosis cases in both groups (group 1, ^{99m}Tc-MAG3; group 2, ^{99m}Tc-DTPA). Such graphs reveal that patients from both groups who were truly diagnosed with obstructive HyN fell in the range of >12 min; this result was in agreement with previous studies (33, 38). The relationship between the elapsed time of the radiopharmaceutical and the T½ readings for patients injected with ^{99m}Tc-MAG3 was as follows: $y = -0.267x + 26.72$; for ^{99m}Tc-DTPA, the equation was $y = -0.226x + 29.35$. This reveals that ^{99m}Tc-MAG3 is also released more rapidly from the kidney than ^{99m}Tc-DTPA, and the research has revealed that this occurs because of two reasons. The first reason is that ^{99m}Tc-MAG3 has a higher extraction efficiency than ^{99m}Tc-DTPA, and the second reason is that ^{99m}Tc-MAG3 has a better response to furosemide (which is injected 15–20 min after the administration of the radiopharmaceutical). Furosemide is a strong diuretic compound to help the obstructed kidney wash the radiopharmaceutical into the urinary bladder. These results are in agreement with previous studies (Jamar et al. 1992, Al-Nahhas et al. 1988). Different pathological examinations of 200 kidneys revealed that non-obstructive HyN affected the right kidney more than the left kidney. The study reveals that HyN is most endemic in Khartoum city. This could result from the high population in Khartoum and the lack of national nuclear medicine centers. The main expected causative factor for HyN is water pollution.

This study concluded that ^{99m}Tc-MAG3 showed lower T½ readings in comparison to ^{99m}Tc-DTPA, which indicates that ^{99m}Tc-MAG3 is cleared faster than ^{99m}Tc-DTPA in all pathological conditions of hydronephrosis (non-obstructive and obstructive HyN

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