ESTIMATION OF GLOMERULAR FILTRATION RATE IN RENAL TRANSPLANTED PATIENTS: COMPARISON BETWEEN ^{99m}TECHNETIUM DTPA GAMMA CAMERA TECHNIQUE AND PLASMA CLEARANCE TECHNIQUE

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ABSTRACT

OBJECTIVE: To find the correlation of glomerular filtration rate (GFR) derived from ^{99m}technetium diethylenetriaminepentaacetic acid (^{99m}Tc DTPA) renography with gamma camera technique and plasma clearance technique in renal transplanted patients and to find the relationship between GFR values from the two techniques.

DESIGN: Descriptive study design with prospective data collection.

SETTING: Department of Radiology, Srinagarind Hospital, Khon Kaen University.

MATERIALS AND METHODS: Ten renal transplanted patients (12 studies) were enrolled into the study between October 2004 and July 2005. GFR was estimated by two different methods, gamma camera technique and plasma clearance technique, using 99mTc DTPA. GFR values derived from the two methods were correlated. The relationship between GFR values from the two techniques is then determined.

RESULTS: We found that there was a fair correlation of the GFR values between the two techniques ($r = 0.69$).

CONCLUSION: Although the GFR value from gamma camera technique may be lower than that of the standard plasma clearance technique, GFR by this method is reliable enough in determining renal function in patients post renal transplantation.

INTRODUCTION

Glomerular filtration rate (GFR) is the most commonly used parameter in determining excretory renal function both in patients with native kidneys and transplanted kidneys. Several techniques have been developed for the estimation of GFR; however some techniques have their own limitations. Although inulin clearance remains the gold standard as a GFR measurement, it requires a steady-state plasma concentration and urine collection, is time-consuming and is also expensive.[1] Endogenous serum creatinine

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clearance, another method for GFR estimation, is not accurate, especially in patients with reduced renal function, due to a compensatory increase in tubular secretion of creatinine.[2] In addition, serum creatinine level depends on muscle mass and is not usually elevated out of the normal range until the GFR has fallen by at least 50%.[3-4]

There are two methods of GFR estimation using radiopharmaceuticals, plasma clearance technique and gamma camera renography. However, the former needs multiple blood samplings and counting for radioactivity. Therefore, gamma camera technique has been more widely used in evaluation of GFR in the clinical practice. Due to most of the data using this method are from the study in native kidneys, we aim to evaluate the correlation of GFR derived from ^{99m}Tc DTPA renography with gamma camera technique and the standard plasma clearance technique in renal transplanted patients.

MATERIALS AND METHODS

The study was approved by the local ethic committee before patient recruitment. Ten renal transplanted patients referred for radionuclide renal function study at Nuclear Medicine Division, Department of Radiology, Srinagarind Hospital between October 2004 and July 2005 were included into the study. Two patients underwent 2 studies giving the total number of 12 studies.

In each patient GFR was studied both by gamma camera technique and plasma clearance technique using ^{99m}Tc DTPA as the radiotracer.

GFR estimation by gamma camera technique

If not contraindicated, the patient was hydrated before commencing the study. Most of the patients had urinary catheter in place. If these were not the cases, they were asked to empty bladder before the study.

After a bolus injection of approximately 3 mCi of ^{99m}Tc DTPA into the anticubital vein of the patient lying in the supine position, the pelvic renal graft dynamic images were acquired using a large field of view, parallel-hole, low-energy collimator equipped with gamma camera (ADAC Genesys, USA) in the anterior projection. A 1-minute pre and post injection counting the radioactivity of the syringe were also performed. In addition, at the end of anterior dynamic imaging of the renal graft, a 1-minute static view of the graft was imaged in the lateral projection and the distance between the center of the graft to the anterior skin surface was measured as a renal depth for subsequent GFR estimation. This renal depth value was later used for attenuation correction in determining the GFR values by Gates technique. The GFR of the gamma camera technique was automatically calculated by the computer program using Gates equation.[5] In brief, the regions of interest were placed at the renal graft and perirenal region inferolaterally to create time-activity curve of each region (Figure 1). Then the net renal curve was acquired by subtraction of the normalized background activity from the renal activity curve. Finally, the area under net renal curve during 2-3 minutes post injection was used to determine the GFR value.

At the end of renal image acquisition, image at the injection site was acquired in every patient. If evidence of radiotracer leakage is found, that particular patient would be excluded from the study.

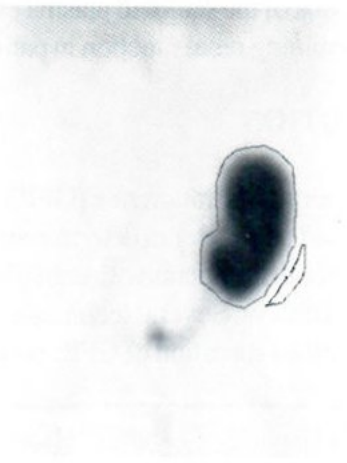

Fig.1 Region of interest of the renal graft and perirenal background.

GFR estimation by plasma clearance technique

During the patient lying for image acquisition in the gamma camera technique, 5-ml of blood was drawn from an anticubital vein of the opposite arm at 10, 20, 30, 60, 120, and 180 minutes after radiotracer injection and collected in the heparinized tube and each specimen was then centrifuged for separation of the plasma. Two-ml plasma was pipetted from each tube and counted for radioactivity. The same was done to the ^{99m}Tc DTPA standardized tube, for the control standard activity.

Plasma radioactivity of each blood sample from 6 points of time of each patient was plotted on a semilogarythmic graph by the Y-axis representing the log scale of the radioactivity and the X-axis representing the linear scale of time, in minute (Figure 2). GFR, or the ^{99m}Tc DTPA clearance, was determined by double exponential analysis with curve peeling technique (Figure 3).

The clearance was calculated by the following equation:

$$GFR = Q0 \times S1 \times S2 / (A1 \times S2) + (A2 \times S1)$$

Q_0 = total amount of 99mTc DTPA injected
= (pre - postinjected syringe weight in gram) x count rate of the standard x 20,000
S_1 = slope of the first exponential function
= 0.693 / T1/2 of the first exponential function
S_2 = slope of the second exponential function
= 0.693 / T1/2 of the second exponential function
A_1 = intercept of the first exponential function
A_2 = intercept of the second exponential function

Correlation of GFR

The two GFR values derived from both techniques were correlated by interclass correlation and regression analysis.

RESULTS

Ten patients, 4 women and 6 men, were studied. The mean age was 42 years (range 15-58). The time between transplantation operation and the time of GFR study ranged from 1 to 7 days (mean 4). GFR values from the two techniques in each patient were shown in Table 1. GFR value by gamma camera method varied from 6.0 to 65.4 ml/minute (mean 26.2), whereas GFR value by plasma clearance technique varied from 25.0 to 85.3 ml/minute (mean 53.4).

Correlation between GFR estimated by gamma camera technique and plasma clearance technique was 0.69 and standard error of estimate was 15.2 ml/minute (Figure 4).

By using regression analysis, the new equation to show the relationship between GFR value of the gamma camera technique (GFR_{ga}) and of the plasma clearance technique (GFR_{pl}) was as followed:

$$GFR_{pl} \text{ in ml/minute} = GFR_{ga} \text{ in ml/minute} \times 0.883 + 30.2$$

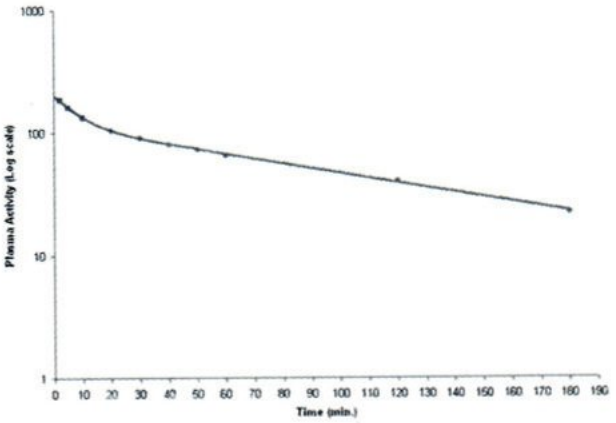

Fig.2 Plasma disappearance curve.

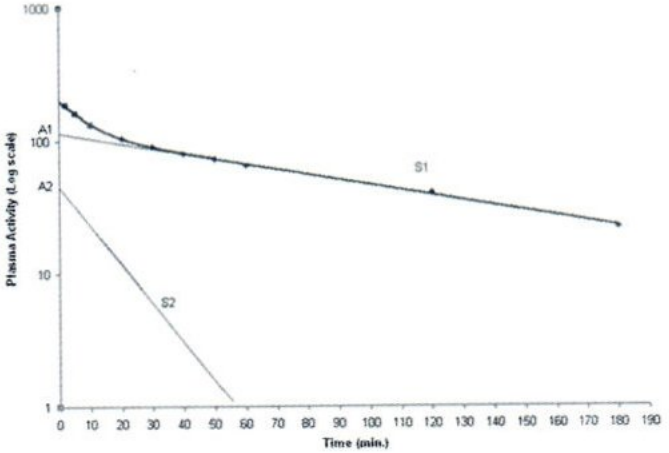

Fig.3 Curve peeling technique

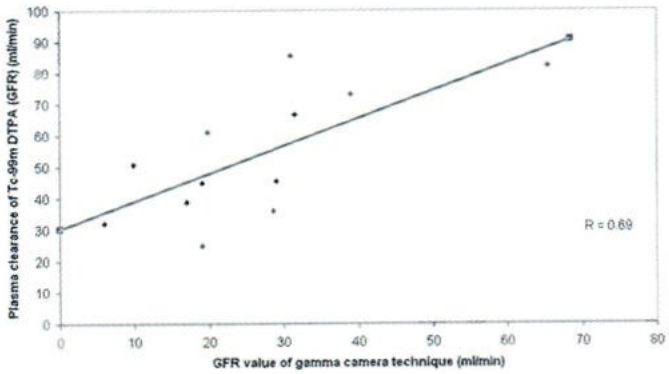

Fig.4 Correlation between GFR values estimated by gamma camera technique and plasma clearance technique.

Table 1 The GFR values derived from both techniques, gamma camera and plasma clearance techniques, using ^{99m}Tc DTPA.

Patient	GFR value by gamma camera technique (ml/min)	GFR value by plasma clearance technique (ml/min)
1	65.4	82.0
2	29.0	45.3
3	9.8	50.8
4	19.9	60.9
5	31.0	85.3
6	31.5	66.7
7	19.0	25.0
8	28.6	36.0
9	39.0	73.0
10	17.0	38.7
11	19.0	45.0
12	6.0	32.0

DISCUSSION

There have been studies showing a fairly good correlation between the GFR derived from gamma camera technique and from plasma clearance technique (r 0.79-0.89).[6-7] However, all of these studies have been conducted in patients with native kidneys. Whether this correlation is still good in the renal transplanted patients still remains unknown.

In this study we found that there was a fair correlation between the GFR values derived from plasma clearance technique and gamma camera renography technique using ^{99m}Tc DTPA in renal transplanted patients (r = 0.69). It should be noted that the GFR value of the gamma camera method was lower than that of the plasma clearance method in every patient studied. This suggests that the GFR estimation from gamma camera technique may not be appropriate for directly applying to the renal transplanted patients. Further regression analysis demonstrated the new equation that showed relationship of the GFR between the two methods. This relationship is useful in converting GFR derived from gamma camera technique, which is widely used in routine clinical practice, into that from a more accurate plasma clearance technique, which demands multiple blood taking and is time consuming.

Estimation of GFR by ^{99m}Tc DTPA gamma camera method using Gates equation bases on the fractional renal accumulation of ^{99m}Tc DTPA during the renal parenchymal phase after tracer injection.[5] By this method, a few parameters influencing the estimated GFR value have to be considered to explain the difference of GFR derived from the two methods. The first one is the fractional renal uptake. The fractional renal uptakes which most correlated with GFR and were used for GFR estimation of Gates equation, were the uptake during 2-3 minutes after ^{99m}Tc DTPA injection. This period of fractional renal uptake derived from the study of native kidneys of Gates model may not be appropriately to be applied to the transplanted kidneys as in our study population. The second factor is the acquisition of renal depth for calculation of attenuation correction. The gamma camera technique with Gates model calculates renal depth from height and weight of the patient giving the distance between the mid-point of kidney to the posterior skin surface at the back. In our study we were aware of this rationale of acquiring renal depth that may not be appropriate in calculating the renal depth of the renal graft while the image acquisition was performed in the anterior pelvic projection. Furthermore, soft tissue swelling at the early post -transplanted period can increase the renal depth; hence applying height and weight should not be accurately applied to this circumstance in measuring the renal depth. Another factor that needs to be considered is the position of the background region of interest to calculate background subtraction.

Since the GFR of plasma clearance technique is basically more accurate than that of the gamma camera technique and GFR derived from gamma camera technique with Gates model may have some limitations in renal transplanted kidney, we propose the relationship to calculate the GFR of plasma clearance technique from that of the gamma camera technique.

However, our study had some limitations. The number of GFR studies is small and the GFR values of these patients were not widely distributed. Most of them were in the low ranges and therefore could not represent a normal distribution of renal transplanted patients with varying renal function. In addition, all of the patients studied were in the early postoperative period, within the first week of transplantation. The result in particular the relationship equation of GFR between the two methods may not be generalized for applying to patients of late follow-up of the renal function. Furthermore, we did not measure the labeling efficiency of ^{99m}Tc DTPA that can affect the accuracy of the acquired GFR value.

We suggest that further researches need to be done in a large scale to evaluate the GFR from these two studies in renal transplanted patients. The fractional renal accumulation of varying time after

^{99m}Tc DTPA injection that most correlates with the GFR value of Gates model should be identified. In addition, the effect of renal depth derived from height and weight method and from the direct measurement of the lateral renal image on the GFR values should be explored.

CONCLUSION

In summary, we have found, in a limited number of patients, a fair correlationship of GFR derived from gamma camera technique and from plasma clearance technique in patients with early post renal transplantation. We also proposed the relationship equation to calculate a more accurate GFR estimation from GFR derived from gamma camera technique commonly performed in our routine clinical practice.

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