Original Article

Renal Allograft Rejection

Renal Allograft Rejection: Role of Tc99m-DTPA Renal Scan

Shafiq Ur Rehman Cheema[1], Sidra Cheema[2] and Sajeel Ejaz[3]

ABSTRACT

Objective: Tc99m- diethylene triamine pentaacitic acid (DTPA) renal renography has been used to evaluate renal transplant function with variable results. In this study we compared the results of renal scan with biopsies of renal allograft to evaluate the ability of renography to differentiate acute rejection from other causes of allograft dysfunction including acute tubular necrosis (ATN) and medication toxicity.

Study Design: Observational / cross sectional study.

Place and Duration of Study: This study was carried out in the Hope Kidney Clinic, Texas, USA from January 1, 2011 to December 31, 2012

Materials and Methods: All renal transplant patients at Hope Kidney Clinic, Laredo, Texas, USA who had Tc99m-DTPA renal scan for elevated serum creatinine and subsequent biopsy within 48 hours were included. A total of eighteen patients underwent allograft biopsy. We tested the hypothesis that decreased flow and function would predict acute rejection and in other etiologies such as ATN normal flow with or without impaired function would be seen.

Results: Four of 9 patients (44%) with impaired flow and function on renography had acute rejection, three of which has vascular component. Four of 9 patients (44%) with normal flow with or without normal function had rejection, none of which has a vascular component.

Conclusion: Based on these findings, it was concluded that Tc99m-DTPA renography is neither sensitive nor specific for the detection of acute allograft rejection butTc99m-DTPA renography may be more sensitive for detecting rejections with vascular component as all of those in this study demonstrated.

Key Words: kidney transplantation; Tc99m-DTPA renography; acute graft rejection, and radionuclide imaging.

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INTRODUCTION

Although episodes of allograft rejection are very common with at least one acute rejection episode in 50-60% renal allograft recipients, diagnosis may be difficult without a biopsy. Nuclear medicine renal scan is commonly used methods in the evaluation of kidney allograft dysfunction[1-4]. Some of the other diagnostic tests used are clinical features, allograft ultrasound, serum renal function tests, MRI and renal biopsy. These investigations help in the recognition of sudden and chronic complications related to kidneytransplantation[5-7]. Nuclear medicine renal scans may show delayed visualization of kidneys. Only limited data is available to assess the role of nuclear scan in detecting acute renal allograft rejection.

[1.] Department of Nephrology / Pathology[2] / Medicine[3], CMH Lahore Medical College, Lahore.

Correspondence: Shafiq Ur Rehman Cheema, Department of Medicine, Division of Nephrology, CMH Lahore Medical College, Lahore.
Contact No.: 0311-2381111
E-mail: shafiqcheema@yahoo.com

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The main objective of this study was to assess the role of renal scintigraphy with ^{99m}Tc-DTPA in the diagnosis of acute renal allograft rejection, when compared to transplant kidney biopsy.

MATERIALS AND METHODS

All renal transplant patients at Hope Kidney Clinic, Laredo, Texas, USA who had A Tc99m-DTPA renography for elevated serum creatinine and subsequent biopsy within 48 hours were included. A total of eighteen patients underwent allograft biopsy over the study period of two years. Transplant recipients' ages ranged from 25 to 62 years with mean age of 47 year, 12 were males (67%) and 4 (23%) were recipients from diseased donors. Kidney biopsy specimens were reviewed by an renal histopathologist according to the Banff 97 classification (13), using a 0 – 3 + semi quantitative scale. We tested the hypothesis that decreased flow and function would predict acute rejection and in other etiologies such as ATN normal flow with or without impaired function would be seen.

Statistical Analysis: Following were calculated: sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV). Kidney biopsy was considered the gold standard for comparison.

Renal Scintigraphic Studies: Details of renal scan findings with normal, acute rejection and ATN are given under the discussion section of this article.

RESULTS

1-*Cases*: Four of 9 patients (44%) with impaired flow and function on renography had acute rejection (Mild=2, Moderate=2), three of which has vascular component. The median time between transplant to biopsy was 1.5 months (range 0.13-3.6).The other five patients had tissue diagnosis of ATN (n=2), thrombotic microangiopathy (n=1), cholesterol emboli (n=1) and chronic allograft nephropathy (n=1).

2-*Controls:* Four of 9 patients (44%) with normal flow with or without normal function had rejection (Mild=2, Moderate=1, Severe=1), none of which has a vascular component. The median time between transplant to biopsy was 5.8 months (range= 2.6-9.6).The other five patients had obstructive uropathy (n=2), Pyelonephritis (n=1), ATN (n=1) and chronic allograft nephropathy (n=1)

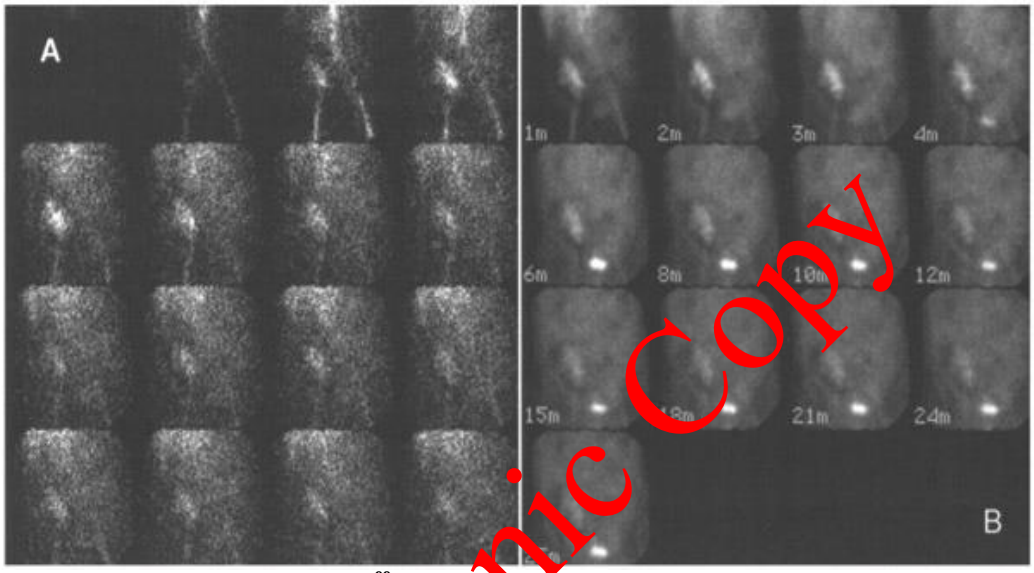

Figure No.1: Renal scientigraphic study with ^{99m}Tc-DTPA of a patient with acute tubular necrosis. A) Flow phase. Note the normal flow to the graft. B) Functional phase. There is mildly reduced accumulation of the radiotracer and moderate reduction of the concentration and excretion of the radiopharmaceutical. A rim of reduce drodioactivity is noted, peripheral to the kidney, peripheral to the kidney, mainly on its lateral border and is due to an hematama.

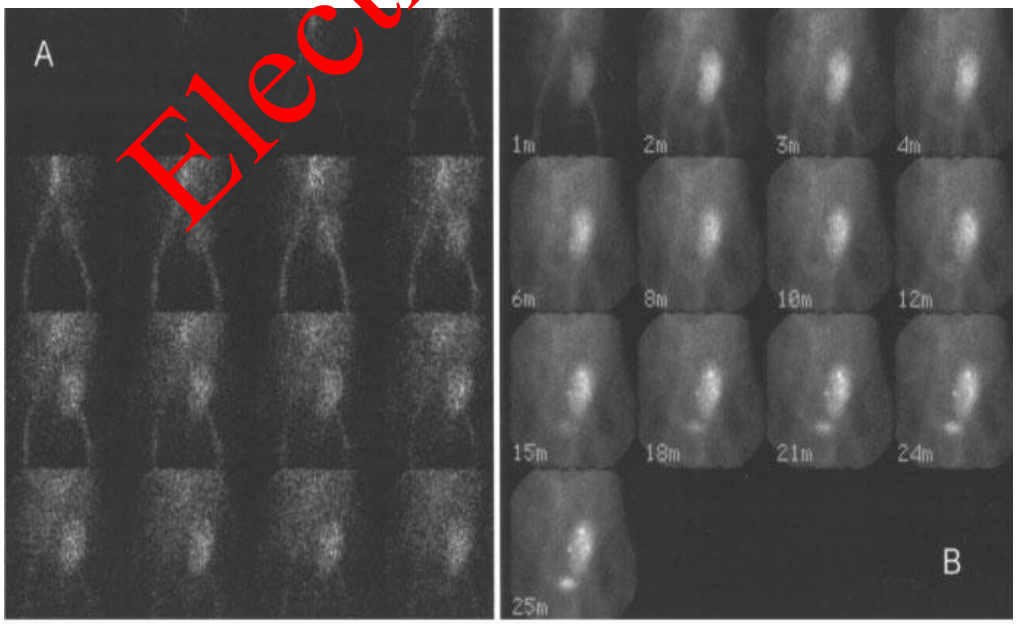

Figure No.2: Renal scintigraphic study with 99mTc-DTPA of a patient with acute rejection. A) Flow phase. Note the moderate reduction of the flow to the graft. There is moderately reduced accumulation, concentration and excretion of the radiotracer.

DISCUSSION

Our results showed Four of 9 patients (44%) with impaired flow and function on renography had acute rejection (Mild=2, Moderate=2), three of which has vascular component. So three out of 4 (75%) with vascular component on biopsy had findings consistent with rejection on renal scan. Our study showed lower sensitivity and specificity of renal scan in detection acute renal allograft rejection. The sensitivity, specificity, positive predictive value and negative predictive value of renal scan in detecting acute rejection was only 50%, 50%, 44% and 55% respectively.

Acute or chronic allograft rejection is a key issue in the follow-up of kidney transplanted recipients since it can cause kidney allograft failure. Several techniques used for the assessment of graft complications are designed for the early diagnosis of rejection. The most commonly used non-invasive methods are serum creatinine levels, glomerular filtration rates, Doppler sonograms, renal scintigraphy (mainly with ^{99m}Tc-DTPA or ^{99m}Tc-MAG_3), magnetic resonance imaging, and serum and immunologic markers. Kidney biopsy is considered the gold standard for accurate determination of kidney allograft dysfunctions.

Tc99m-DTPA renography plays a crucial role in the study of renal graft dysfunctions[8]. Routinely, ^{99m}Tc-DTPA or ^{99m}Tc-MAG_3 is used[9-11]. The nuclear medicine assessment of renal allograft involves detailed analysis of the 3 phases of renal scan: the flow phase, the functional phase and the excretion phase (4, 12).^{99m}Tc-DTPA can be extremely useful in the evaluation of dysfunctional kidneys, since it has a reasonable extraction rate and a low cost.

Kidney biopsy on the other hand is considered the gold standard for the detection of renal graft complications. But kidney biopsy is an invasive test with a higher morbidity when compared to non-invasive diagnostic tests such as nuclear renal scan. Kidney biopsy should be performed only when non-invasive procedures are indeterminate. The overall precision of kidney biopsy has been reported to be more than 90 %[13,14].

Renal allograft dysfunction can be evaluated with filtered or tubular secreted radiopharmaceuticals using a three-phase approach. The phase one assesses the perfusion and is also known as the angiographic phase or the first-pass study. The phase two reflects the physiologic mode of clearance of that radiopharmaceutical (i.e., filtered of secreted). The third phase is the excretory phase, which reflects the glomerular filtration rate (GFR) and permits an assessment of the integrity of the genitourinary system.

Classically, *acute rejection* appears on nuclear medicine ^{99m}Tc-DTPA as delayed transplant visualization (decreased perfusion) on the first-pass renal scintianogiography phase, with poor parenchymal uptake and high background activity (poor renal function and clearance) in the second and third phases. Transplant rejections may also be detected by a number of static imaging techniques.

On nuclear medicine imaging studies, *ATN* typically shows good renal perfusion on the first-pass phase with ^{99m}Tc DTPA. On the second and third phases, ^{99m}Tc DTPA show poor parenchymal accumulation and wash-out of the radiotracer as a result of decreased glomerular filtration. In addition, high surrounding tissue background activity is seen as a result of poor overall plasma clearance of the radiotracer. In the third phase, however, there is a similar poor wash-out of the accumulated renal parenchymal activity as a result of diminished glomerular filtration. These findings are consistent with the pathophysiology of ATN, in which renal blood flow is preserved relative to glomerular filtration[15].

Our study findings were different from Adelina S. et al[16]. In this study the scintigraphic results were concordant with the biopsies in 86% of the cases studied. The sensitivities of renal scintigraphy for detection of acute tubular necrosis, acute allograft rejection (AR) and renal cortical necrosis (CN) were 98%, 87% and 100%, respectively. In the same study specificities and accuracies for detection of ATN, AR and CN were 89%, 86% and 100%, and 95%, 87% and 100%, respectively. It was concluded 99mTc-DTPA renal scan showed a good overall accuracy in the detection of acute renal graft complications. It can be used as a dependable tool in the regular evaluation of renal transplant recipients. But our study showed lower sensitivity and specificity of renal scan in detection acute renal allograft rejection. The sensitivity, specificity, positive predictive value and negative predictive value of renal scan in detecting acute rejection was only 50%, 50%, 44% and 55% respectively.

Accurate non-invasive methods to diagnose kidney dysfunctions, at a lower cost are the ideal techniques to be used. Delaney et al.[17] compared kidney biopsy, Doppler ultrasound and nuclear medicine renal scans for the detection of renal graft complications and also performed a cost analysis. Renal scan was the most sensitive method for detection of acute rejection (70% overall), while kidney biopsy and Doppler ultrasound had sensitivities as low as 52% and 43%, respectively. The cost of radionuclide scintigraphy was not ideal (only 9% lower than core biopsy).

Hall et al.[18] also compared renal allograft scintigraphy and ultrasound to biopsy findings. In this study ultrasound and renal scan was done within two days of kidney biopsy. They found out that renal allograft scintigraphy had a sensitivity of 96% for the detection of acute rejection while the sensitivity of ultrasound was just 21%. However, the specificity of scintigraphy was low at 54%.

Akhtar et al.[19] conducted a study looking at the sensitivity and specificity of Doppler ultrasound. They found that overall sensitivity and specificity of Doppler ultrasound was low for the detection of AR, ATN or cyclosporine toxicity. In another study, Aktas et al.[20] reported Doppler ultrasound sensitivities was low for low-grade rejection and as high as 88% for high-grade rejections.

Again, our study showed much lower sensitivity and specificity of renal scan in detection acute renal allograft rejection as compared the aforementioned studies. The sensitivity and specificity of renal scan in detecting acute rejection was only 50% in our study.

Khajehmugehi et al.[13] concluded after reviewing 230 episodes of AR in renal transplant recipients, that although the most sensitive (91%) way to diagnose AR was kidney biopsy, "the best mode of diagnosing rejection was DTPA isotope scanning." However, only the kidney biopsy can give the diagnosis and severity of the acute rejection, especially in cases when ATN is coupled with rejection or in presence of a vascular component of rejection.

Our study has limited number of patients. More studies and multicenter trials should be conducted to illustrate the benefits of noninvasive and preferred techniques so that core kidney biopsy with potential complications could be avoided.

CONCLUSION

1- Tc99m-DTPA renography is neither sensitive nor specific for the detection of acute allograft rejection.

2- Tc99m-DTPA renography may be more sensitive for detecting rejections with vascular component as all of those in this study demonstrated.

3. Kidney Biopsy remains the gold standard to diagnose, assess the severity of rejection and to rule out other potential causes of renal allograft dysfunction.

Conflict of Interest: The study has no conflict of interest to declare by any author.

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