THE DIAGNOSTIC ROLE OF ENALAPRIL RENAL SCINTIGRAPHY IN PATIENTS WITH SUSPECTED RENOVASCULAR HYPERTENSION

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SUMMARY : The aim of this study was to investigate the sensitivity and specificity of enalapril renal scintigraphy using 99m Technetium-diethylenetriaminepentaacetic acid (99k Tc-DTPA) for detecting renal artery stenosis in subjects with suspected renovascular hypertension. Twenty-seven subjects (13 female, 14 male, mean age : 34.9 ± 7.8) were studied with baseline and enalapril enhanced 99m Tc-DTPA renal scintigraphy. Subsequently, all patients underwent renal angiography and scan interpretations were compared with renal arteriography results. Ten patients were diagnosed to have renal artery stenosis based on the renal scintigraphy findings. These findings included reduced glomerular filtration rate, reduced split renal function and abnormal time activity curves following enalapril administration. Renal artery stenosis was demonstrated by renal angiography in 9 of these patients. Seventeen patients who had normal renal scintigraphic examinations, also had normal renal arteries demonstrated by renal angiography. The results of this study revealed that enalapril renal scintigraphy provides a useful noninvasive test for the detection of renal artery stenosis in patients with suspected renovascular hypertension, with a sensitivity of 100% and specificity of 94%. Negative findings in scintigraphy were sufficient to rule out the diagnosis. Psitive findings highly suggestive of renal artery stenosis, however, need to be confirmed by renal angiography.

***Key Words** : Renal Scintigraphy, Enalapril, 99m Technetium Diethlentriaminepentaacetic Acid, Renal Artery Stenosis.*

INTRODUCTION

The prevalence of renovascular hypertension (RVH) ranges from 0.5 to 5% in general hypertensive population (1) and increases up to 45% in patients with accelerated and malignant hypertension (2). Since it is potentially curable by surgery or angioplasty, its early diagnosis is important. A reliable, noninvasive test for RVH with or without angiotensin converting enzyme (ACE) inhibitors has been used as a diagnostic test for RVH or renal artery stenosis (RAS).

In patients with RVH renin angiotension-aldostrone system is activated due to hypoperfusion of the kidneys. Angitensin II causes vasoconstriction on efferent arteriole of glomerulus, so the filtration pressure and glomerular filtration rate is restored. ACE inhibitors block the formation of Angiotensin II, resulting in decreased filtration pressure and filtration rate in patients with RVH. These changes in renal function can be shown by renal

scintigraphy combined with ACE inhibitors.

The aim of this study was to investigate the sensitivity and specificity of enalapril renal scintigraphy using 99mTechnetium-diethylenetriaminepentaacetic acid (99mTc-DTPA) for detecting renal artery stenosis in subjects with suspected renovascular hypertension.

MATERIALS AND METHODS

Subjects : The study group consisted of 27 hypertensive patients having diastolic blood pressures over 100 mmHg with suspected renovascular pathology. There were 13 female and 14 male patients with a mean age of 34.9 ± 7.8 years. Plasma creatinine, BUN, electrolyte levels and creatinine clearance were determined as standard renal function tests. All hypertensive medications were withheld at least 48 hours before scintigraphy. All patients were hydrated well before the scintigraphy was performed.

Renal hemodynamics : For the baseline study, patients were placed in supine position under a gamma camera (Toshiba 501 GCA) equipped with an all-purpose, low energy, parallel hole collimator. Kit formulation of DTPA was prepared according to the manufacturers' recommendation. Following i.v. administration of 370 MBq Tc-99m-DTPA serial renal images were recorded at a rate of one frame/sec for 120 seconds and one frame/15 seconds for 20 minutes in a matrix size of 64x64.

Forty-eight hours after the baseline study, renal scintigraphy was repeated following oral administration of 20 mg Enalapril and a subsequent lapse of 2 hours.

Scintigraphic analysis : Visual renographic analysis, glomerular filtration rate (GFR), time to maximum activity (Tmax), half time of the maximum activity (T 1/2), split renal function (SRF) were evaluated as diagnostic parameters.

Visually, the kidney size, shape, its tracer uptake and appearence of the tracer in the pelvicalyceal system and renogram curves were evaluated and compared before and after enalapril. Using the region of interest (ROI) method, renal regions, abdominal aorta and surrounding backgrournd regions were drawn. Time activity curves of the kidneys and aorta were obtained using background substraction technique. T max and T1/2, were calculated using the time activity curves of each kidney. The injected dose was measured by counting the syringe with a gamma camera using standardized geometry. To calculate global and split GFR, the fractional uptake was determined by the computer. GFR was calculated according to the Gates' method (14). Reno index (SRI, split renal function) values of kidney were defined as the percentage contribution of each kidney to total renal radioactivity (as a proportion of total GFR) calculated over the first 2-3 min. after dose injection.

Pre (B) and post enalapril (E) data and differences between them were evaluated separately by two experienced physicians. Following the scintigraphic examination all patients were examined by digital substaction angiography (DSA) and/or selective angiography to document the renal vascular status. Angiographic results were compared with scintigraphic findings.

Angiographic Method : A no : 5 French i.v. digital substraction angiography (DSA) catheter was placed into the right atrium via an antecubital vein (21 subjects). A selective renal angiography was performed in six patients, whose, i.v. renal DSAs were not diagnostic.

Statistical analysis : All data were expressed as mean and standard deviation. The significance of the difference between the parameters before and after enalapril were tested for stenotic and normal kidneys using Wilcoxon-signed rank analysis and paired t test respectively.

RESULTS

Seven of the 27 patients who had normal sized kidneys were diagnosied to have RAS according to their scintigraphic findings. Additonaly, 3 patients who had unilateral atrophic kidneys,were also interpreted as having RAS. In the latter group of patients,whether the kidney atrophy was the primary event or socondary to RAS could not be determined.The renal scintigraphies of the remaining 17 patients were interpreted as normal. Subsequent renal angiographies of the 27 patients showed that 9 of them had renal artery stenosis. All of the 3 patients who had atrophic kidneys in scintigraphy were shown to have renal artery stenosis in angiography and therefore the final diagnosis was renal atrophy secondary to renal artery stenosis and RVH . The remaining 6 patients who had renal artery stenosis in angiography were also diagnosed to have RAS by scintigraphy. One patient who seemed to have RAS in scintigraphic evaluation had normal findings in angiography. All of the 17 patients who had normal

findings in scintigraphy were also normal in angiographic examination.

According to these results the sensitivity and the specificity of the scintigraphic evaluation in RAS were found to be 100 % and 94 % respectively.

Enalapril administration did not change the mean GFR and SRF values significantly in patients with normal renal arteries (Table 1). In patients with renal artery stenosis and normal sized kidneys, enalapril reduced the mean GFR and SRF values significantly (Table 1). The effect of enalapril on Tmax and T1/2 was insignificant in both groups (Table 1). In patients with renal artery stenosis and atrophic kidneys, the mean GFR and SRF values did not decrease, but slightly increased, following enalapril administration (Table 2). This was in contrast to the findings of the patients with renal artery stenosis with normal sized kidneys.

DISCUSSION

There are several ACE inhibitors used clinically in the treatment of hypertension. However, captopril is the only one, to the best of our knowledge, that has been combined with renal scintigraphy in the diagnosis of RAS or RVH. Enalapril is a more recent ACE inhibitor, and various possible side effects of captopril, such as neutropenia, nephrotic syndrome, taste loss and skin rashes are rarely seen with enalapril (3, 4).

A comparison of enalapril and captopril renal scintigraphies in regard to their sensitivity and specificity ratios would be important before suggesting the use of enalapril for the diagnostic purposes.

There are many factors effecting the sensitivity and specificity obtained in similar studies rendering their comparison difficult.Most important of these include the various diagnostic criteria used,and how the diagnosis of RAS or RVH was verified.The demostration of RAS in a hypertensive patient is highly suggestive of RVH, however, the classical definition of RVH , is based on retrospective diagnosis requiring hypertension cure or improvement after stenosis correction (5). In many studies like ours the scintigraphic diagnosis was later verified with renal angiography. Therefore the diagnosis of RAS was confirmed.

	BASELINE ENALAPRIL			BASELINE ENALAPRIL		
	STENOTIC 6 kidneys	STENOTIC 6 kidneys	P VALUE	NORMAL 42 kidneys	NORMAL 42 kidneys	P VALUE
GFR (ml/min)	41.9 ± 19	30.43 ± 17	0.04[a]	43.47 ± 15	41.48 ± 11	> 0.05
SRF (%)	41.43 ± 9.3 4	35.14 ± 11.3	0.02[a]	51.02 ± 7	51.8 ± 7.8	> 0.05
T max (min)	9 ± 4.27	10.15 ± 3.64	> 0.05	3.94 ± 1.78	4.38 ± 3.14	> 0.05
T1/2 (min)	9.77 ± 2.96	8.73 ± 5.06	> 0.05	9.95 ± 5.53	9.48 ± 3.75	> 0.05

a statistically significant.

Table 1 : The mean ± std values of kidneys before and after enalapril (excluding 3 atrophic stenotic kidneys) for the GFR, SRF, Tmax, T1/2 parameters.

	BASELINE STENOTIC 3 kidneys	ENALAPRIL STENOTIC 3 kidneys
GFR (ml/min)	15.6 ± 10.57	20.07 ± 10.9
SRF (%)	21.17 ± 11.91	24.73 ± 10.42

Table 2 : The mean ± std values of 3 atrophic stenotic kidneys before and after enalapril for the GFR, SRF, Tmax, T1/2 parameters.

In a recent review by Prigent (5), the mean sensitivity and specificity ratios of captopril renal scintigraphy in diagnosis of RAS were found as % 73 and % 90 respectively. The studies we reviewed (6, 7, 8, 9, 10, 11, 12, 13, 14), utilized an analysis method based on comparing the pre and post captopril renal scintigraphies. Wen the scintigraphic analysis

was based on the post captorpril study only (8, 9, 10, 11, 13), mean sensitivitiy and specificity ratios were %85 and %83 respectively (5).

The results of these studies reveal that the sensitivity of captopril renal scintigraphy has a tendency to increase if the scintigraphic diagnosis is based on the analysis of post captopril study only. The reverse is true for specificity and it increases when the diagnosis is based on anaysis of captopril induced changes between pre and post captopril renal scintigraphies.

Since both enalapril and captopril have the same mechanism of action, the high sensitivity ratio (100 %) in diagnosing RAS obtained in our study is unlikely to be explained by different ACE inhibitor selection. The major factor increasing the sensitivity ratio is probably the inclusion of the 3 patients with small sized kidneys into the group of patients diagnosed as RAS.

These patients were included simply because, we could not exclude the possibility that they could have RAS. It is our opinion that the main role of ACE inhibitor renal scintigraphy in RVH, is its ability of excluding the diagnosis of RVH. Establishing a diagnosis of RVH requires verification by improvement in hypertension following stenosis correction. Therefore ACE inhibitor renal scintigraphy must attain a high sensitivity ratio, while its specificity is of secondary importance. Post ACE inhibitor renal scintigraphy alone can be better used for this purpose. The high specificity ratio obtained in our study can be expected to decrease, if a greater number of patients is employed.

The results of this study showed that enalapril Tc-99m-DTPA renal scintigraphy can be used as a diagnostic test in patients with suspected RVH.

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