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Acute Protein Loading In The Assessment Of Renal Reserve

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Summary

Functional renal reserve is a measure of the capacity of the kidney to increase the glomerular filtration in response to the stimulus of a protein meal or amino acid infusion. The aim of this study was to evaluate the usefulness of protein meal test to measure functional renal reserve in normal subjects and various groups of renal patients. One hundred and twenty five subjects from the Nephrology Clinic, Kuala Lumpur General Hospital were subjected to a protein loading test to measure their renal reserve. Each subject had to eat a 100 gram cooked chicken meat and timed 2 hours urine collections before and after the test meal were done to measure the creatinine clearances. The 62 healthy subjects showed a mean renal reserve (creatinine clearance after protein loading - baseline creatinine clearance) of 31.0 ml/min. The 31 subejcts with various kidney diseases showed a mean renal reserve of 13.5 ml/min. The 19 renal transplant recipients showed renal reserve of 13.2 ml/min. The 12 nephrectomised donors showed renal reserve of 5.4ml/min. Renal reserve may be used to assess suitability of living related transplant donor for nephrectomy.

Key words: Protein loading test, Renal reserve.

Introduction

The normal kidney has a functional reserve and this reserve enables the body to cope with increased demand in certain situations i.e. pregnancy, burns etc[1]. This concept becomes more important when renal transplantation on living related kidney donors produces a group of individuals with a single kidney in whom the renal functional reserve is expected to decrease. The extent to which the individual is affected by this has been the subject of many studies. After 20 years it is now known that there is no significant increased incidence of hypertension and late proteinuria in the kidney donors[2].

In the classic paper by Brenner, chronic protein loading had been demonstrated to cause glomerular hyperfiltration with eventual progression to glomerulosclerosis[3]. It was Bosch however who proposed the use of oral protein loading to measure renal reserve[4,5]. This has the advantages of simplicity of administration, cost-effectiveness and reproducibility.

The aims of the study were as follows:

1. To evaluate the usefulness of acute protein loading as a method of measuring functional renal reserve.

2. To measure renal reserve in normal subjects, subjects with kidney diseases, kidney donors and transplant recipients.

Materials and Methods

Four groups of subjects were studied. The first two groups of subjects were recruited from 1.4.1987 to 31.12.1988 over a 21 month period. Sixty two were normal healthy subjects and 32 were subjects with various kidney diseases followed up at the nephrology clinic Kuala Lumpur General Hospital. The diagnosis of the group with kidney diseases consisted of biopsy proven glomerulonephritis, non-biopsy proven glomerulonephritis, obstructive uropathy, polycystic kidney, diabetic nephropathy, hypertensive nephropathy and gouty nephropathy. The other two groups of subjects were recruited from 1.9.1991 to 31.9.1991 over a one month period. Twelve of them were kidney donors and 19 of them were kidney transplant recipients.

Each group of subjects underwent thorough physical examination and a urine sample was send for light microscopy. The dietary history of each patient was assessed by a dietician. On the day of study, a 2 hour urine collection was started at 0830 before protein ingestion and another collection was made at 1330 after protein ingestion for estimation of creatinine clearance. Blood was taken for creatinine, urea and uric acid at the middle of each urine collection. A 100gm cooked chicken meat was given to each subject at 1100 and each subject was instructed to consumed it within half an hour. Creatinine clearances were corrected for 1.73 meter square surface area. Statistical analysis were done using both student "t" test and Mann Whitney "U" test for comparison and chi square wherever applicable.

Results

The general characteristics of all subjects are as show in (Table 1). The age of the subjects ranged from 20 to 69 years old. The blood pressures were higher in the group with kidney diseases. There was no difference in the daily protein intake among the four groups of subjects.

The mean serum creatinine of healthy subjects, subjects with kidney diseases, kidney donors and kidney transplant recipients were significantly elevated after protein loading (Table II).

The renal reserve (creatinine clearance after protein loading - baseline creatinine clearance) of healthy subjects, subjects with kidney diseases, kidney donors and kidney transplant recipients were 31.0 ml/min, 13.5 ml/min, 5.4 ml/min and 13.2 ml/min respectively.

There was a trend of greater change of creatinine clearance after protein loading with a lower baseline creatinine clearance in all four groups of subjects indicating a greater renal reserve with lower creatinine clearance. (Table III) An analysis of daily dietary protein intake of each subject indicated an increase in baseline creatinine clearance with higher protein intake. (Table IV)

Discussion

In our study all subjects tolerated the protein test meal well. The 100gm of protein test meal used

Table 1
General characteristics of normal subjects, subjects with kidney disease, kidney donors and kidney transplant recipients

	Normal n=64	Kidney Diseases n=30	Kidney Donors n=12	Kidney Recipients n=19
Age (years)	39.4 ± 11.0 (20-63)	46.8 ± 14.5 (20-69)	53.1 ± 6.7 (41-64)	34.1 ± 2.4 (20-53)
Sex				
male	36	23	5	9
female	26	9	7	10
Race				
Malay	28	11	5	6
Chinese	16	15	4	9
Indian	18	6	3	4
Blood pressure (mmhg)				
*syst.	116.6 ± 12.9 (90-150)	150.6 ± 20.8 (120-200)	140.0 ± 18.4 (110-170)	130.6 ± 13.6 (110-160)
*diast.	74.9 ± 8.5 (60-100)	88.8 ± 13.6 (70-120)	82.7 ± 7.9 (70-100)	87.1 ± 9.2 (70-100)
Daily dietary protein (gm/day)	56.7 ± 14.2 (35.0-88.4)	56.5 ± 12.0 (34.0-89.2)	62.5 ± 17.3 (31.9-82.6)	65.7 ± 22.3 (26.0-105)

**syst – systolic, diast – diastolic*

is comparable in amount with 80 - 150gm of protein test meal employed in other studies[5,6]. The timed collections of urine creatinine estimation has the advantage of both ease of supervision and obviating the need for hospitalization. The amount of urine flow was adequate and this was ensured by encouraging large amounts of oral fluid during the test period.

The estimation of glomerular filtration rate by creatinine clearance is the usual method of measuring the glomerular filtration rate in clinical practice although it is well recognised that an element of error is introduced by contribution of tubular secretion to the urinary creatinine. The importance of the contribution increases when the glomerular filtration rate is severely depressed[7]. This consideration would apply to a small number of subjects in the group with kidney diseases. However, this study was concerned with variations from an unstimulated level rather than with absolute values. In other studies it was also found that in the estimation of glomerular filtration after protein loading the use of creatinine and inulin clearances gave similar results and concluded that the former is a reliable indicator of these changes[5].

Table II
Laboratory results before and after protein loading in normal subjects and subjects with kidney disease

Laboratory results	Before	After	p
Normal subjects			
Creatinine (umol/l)	91.6 ± 22.8 (61 – 163)	124.3 ± 30.6 (66 – 189)	<0.00000001
Creatinine clearance (ml/min)	96.2 ± 26.7 (47 – 153)	127.2 ± 50.0 (56 – 264)	<0.00001
Urea (mmol/l)	3.99 ± 1.00 (2.1 – 6.8)	4.65 ± 0.88 (2.8 – 6.4)	<0.0001
Uric acid (umol/l)	374.7 ± 72.7 (241 – 574)	423.4 ± 79.3 (223 – 583)	<0.001
Subjects with kidney diseases			
Creatinine (umol/l)	268.5 ± 157.3 (112 – 675)	310 ± 151.5 (164 – 710)	ns
Creatinine clearance (ml/min)	38.3 ± 27.8 (1 – 108)	51.8 ± 36.1 (8 – 192)	<0.05
Urea (mmol/l)	11.0 ± 5.4 (5.0 – 26.0)	11.4 ± 5.4 (5.1 – 26.8)	ns
Uric acid (umol/l)	492.3 ± 127.1 (269 – 639)	532.6 ± 151.9 (270 – 786)	ns
Kidney donors			
Creatinine (umol/l)	139.3 ± 40.0 (92 – 218)	172.0 ± 25.4 (123 – 204)	<0.001
Creatinine clearance (ml/min)	66.4 ± 23.6 (13.8 – 94.2)	71.8 ± 23.2 (43.9 – 113)	ns
Urea (mmol/l)	5.3 ± 1.4 (3.5 – 8.0)	6.2 ± 1.6 (3.7 – 9.5)	ns
Uric acid (umol/l)	439.8 ± 97.9 (285 – 580)	496.2 ± 102.6 (314 – 636)	ns
Kidney transplant recipients			
Creatinine (umol/l)	104.9 ± 18.8 (73 – 137)	156.4 ± 28.8 (116 – 220)	<0.001
Creatinine clearance (ml/min)	73.5 ± 27.0 (32.8 – 117.6)	86.7 ± 46.4 (33 – 208.8)	ns
Urea (mmol/l)	4.7 ± 1.0 (3.7 – 6.7)	5.8 ± 1.2 (3.5 – 7.6)	ns
Uric acid (umol/l)	401.7 ± 60.1 (198 – 579)	517.4 ± 91.7 (383 – 687)	ns

Table III
Degree of change in creatinine clearance (Crc) after protein loading in association with baseline creatinine clearance in normal subjects, subjects with kidney disease, kidney donors and kidney transplant recipients

Baseline Crc (ml/min)	No. of subjects	Crc after protein loading	Degree of change (%)
Normal subjects			
<70	10	125.7 ± 38.8 (72.0 – 179.0)	143
70-99	19	118.5 ± 48.7 (56.0 – 160.0)	41
100-129	29	132.4 ± 38.3 (81.0 – 228.0)	17
>130	4	134.5 ± 30.7 (91.0 – 162.0)	-4
Subjects with kidney diseases			
<40	16	29.7 ± 17.1 (8.0 – 65.0)	99
40-69	11	62.7 ± 16.8 (20.0 – 84.0)	20
>70	5	98.8 ± 56.9 (54.0 – 192.0)	19
Kidney donors			
<60	4	57.3 ± 11.8 (44.9 – 66.0)	39
60-90	6	72.4 ± 9.1 (20.0 – 84.0)	-2
>90	2	99.0 ± 19.8 (85.0 – 113.0)	7
Kidney transplant recipients			
<60	8	70.0 ± 33.0 (44.9 – 66.0)	48
60-90	5	82.1 ± 40.4 (41.4 – 141.6)	6
>90	6	112.9 ± 64.0 (46.8 – 208.8)	7

*Degree of change = creatinine clearance after protein loading - baseline creatinine clearance / baseline creatinine clearance x 100

Table IV
Total daily dietary protein in association with baseline creatinine clearance(Crc) in normal subjects, subjects with kidney disease, kidney donors and kidney transplant recipients

Baseline ml/min	Crc No. of subjects	Daily dietary protein (gm/day)
Normal subjects		
< 70	10	50.2 ± 11.4 (38.8 – 72.6)
70-99	19	57.3 ± 19.4 (31.9 – 82.6)
100-129	29	63.4 ± 11.7 (50.0 – 88.4)
>130	4	47.1 ± 15.3 (36.3 – 57.9)
Subject with kidney diseases		
< 40	16	56.4 ± 14.6 (34.0 – 89.2)
40-69	11	60.1 ± 7.1 (52.9 – 71.2)
>70	5	52.7 ± 10.6 (41.5 – 62.5)
Kidney donors		
< 60	3	70.3 ± 17.5 (57.9 – 82.6)
60-80	5	51.1 ± 27.1 (31.9 – 70.2)
>80	4	66.2 ± 7.5 (60.9 – 71.2)
Kidney transplant recipients		
< 60	8	69.3 ± 28.1 (26.0 – 105.0)
60-90	5	72.6 ± 17.6 (55.0 – 93.0)
>90	6	55.2 ± 15.2 (37.0 – 75.0)

The timing of measuring the postprandial creatinine clearance 2 hours after meal was chosen because the maximal increase in glomerular filtration rate after an oral load of protein occurs 100-120 minutes after ingestion[5]

The underlying mechanism of the increase in glomerular filtration after protein loading is unknown. Chan *et al* suggested that there is post prandial renal vasodilatation[8]. This renal vasodilatation could be a result of several factors which included post absorptive entry into circulation of amino acids[9], enhanced secretion of glucagon[10] and the release from storage sites in the liver of a vasodilator substance known as glomerulopressin (still unidentified)[11,12,13].

The magnitude of renal reserve measured in this study, 31 ml/min for healthy subjects, 13.5 ml/min for subjects with kidney diseases and 13.2 ml/min for kidney transplant recipients compared very well with figures from other studies with 34 - 53 ml/min[5,6] for healthy subjects, 0 - 16 mil/min[5,14]

for subjects with kidney diseases and 15 -18 ml/min[15] for kidney transplant recipients. The 5.4 ml/min renal reserves for kidney donors in this study is lower compared to other studies i.e. 12 - 19 ml/min[5,16]. The younger mean age of the kidney donors (36.6 years old) in one of the reference studies[5] could account for this difference.

The estimation of renal reserve has certain potential clinical value. Measurement of renal reserve preoperatively for patients undergoing nephrectomy may predict the post operative renal function and patient with poor reserve may be advice to defer the operation.

A review of 3 of our kidney donors with nephrectomy done in 1987 showed that the first 2 subjects with serum creatinine of 70 umol/l and 44 umol/l and renal reserve of 84 ml/min and 24 ml/min respectively prior to nephrectomy had serum creatinine of 92 umol/l and 150 umol/l and renal reserve of 17 ml/min and 0 ml/min 4 years post-nephrectomy. The last subject with serum creatinine of 124 umol/l, creatinine clearance of 85 ml/min and no renal reserve (creatinine clearance decrease after protein loading) had impaired serum creatinine of 218 umol/l, creatinine clearance of 62.8 umol/l and no renal reserve 4 years post-nephrectomy.

In conclusion, this study confirmed the value of acute protein loading as a measurement of functional renal reserve and this is particularly useful to assess suitability of living related donors for nephrectomy.

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