Which routine test for kidney function?

A PARKIN, H C SMITH,* AND J T BROCKLEBANK*

*Department of Medical Physics and *University Department of Paediatrics, St James's University Hospital, Leeds*

SUMMARY Eighty measurements of plasma creatinine concentration, height:creatinine ratio, and plasma β_2 microglobulin concentration were made on 72 children (age 4 months–18.5 years) with known renal disease. Results were compared with simultaneous measurements of glomerular filtration rate using plasma clearance of ^{51}Cr edetic acid to assess the performance of each test as an initial screening procedure of renal insufficiency. Height:creatinine index <2.1 was found to have a higher sensitivity and predictive value of a normal result than the other tests and is therefore the preferred test for a screening procedure.

A simple reliable method of measuring glomerular filtration rate is important in the routine assessment of children with renal disease. The creatinine clearance test is inherently inaccurate with poor reproducibility.¹ Radionuclide clearance methods are more accurate but available only in specialised centres. Therefore, the plasma creatinine alone is used in the routine assessment of glomerular filtration rate. In children, as plasma creatinine concentration changes with age, correction is made for changes due to growth by calculating a height:creatinine index, which has some advantages.²

There is an inverse relationship between plasma β_2 microglobulin concentration and glomerular filtration rate and it has been suggested that this is used to measure glomerular filtration rate.³ In contrast with creatinine its plasma concentration is unaffected by diet¹ but its production is enhanced by active infection or malignancy.

The aim of this study was to compare the sensitivities and predictive values of plasma concentration, height:creatinine index, and plasma β_2 microglobulin as methods of assessing glomerular filtration rate using plasma clearance of ^{51}Cr edetic acid as a 'gold standard' so that recommendations can be made to the non-nephrologist for the test that is most helpful for routine clinical use.

Patients and methods

Seventy two children known to have renal disease were studied. There were 33 girls and 39 boys aged between 4 months and 18.5 years. Four of these children had two measurements and a further two

had three measurements after intervals of several months making 80 observations in total. All the children were weighed, their heights measured using a Harpenden stadiometer, and their surface areas calculated using the Dubois formula.⁴ Fasting plasma creatinine concentration was measured by a kinetic Jaffe reaction using a Rank Elger Chemspeck autoanalyser. The β_2 microglobulin was measured by radioimmunoassay (Phadebas (R) B2 microtest, Pharmacia Diagnostics). Sera were stored at -20°C before analysis.

Glomerular filtration rate was calculated from the plasma clearance of ^{51}Cr edetic acid using standard methods.⁵ Results were corrected to 1.73 m^2 body surface area before analysis.

Impaired renal function was defined as a plasma clearance of ^{51}Cr edetic acid of less than $80\text{ ml/min}/1.73\text{ m}^2$ in children over 3 years. In those under 3 years when normally glomerular filtration rate changes with age, renal impairment was defined as clearance more than two standard deviations below the published mean for age.⁶

Normal plasma creatinine concentration has a log normal distribution.¹ All analysis were therefore performed after logarithmic transformation and standard statistical methods were applied.

Results

The mean coefficient of variation of the creatinine measurement at a plasma concentration of $70\text{ }\mu\text{mol/l}$ was 8% and of β_2 microglobulin was 6% on both repeated measurements of the same sample and repeated samples from the same patient. The

Figure Distribution of height:creatinine and clearance of ^{51}Cr edetic acid in all patients.

reproducibility of the plasma clearance of ^{51}Cr edetic acid in six healthy adults was 4%.

The plasma clearance of ^{51}Cr edetic acid was greater than 80 ml/min/1.73 m² in 58 measurements (mean (SD) 140 (28)). There was a linear relationship between plasma clearance of ^{51}Cr edetic acid and 1/creatinine, 1/ β_2 microglobulin, and height:creatinine index with correlation coefficients of 0.88, 0.87, and 0.85 respectively. The distribution of plasma clearance of ^{51}Cr edetic acid and height:creatinine index for the patients studied is shown in the figure. The geometric means and ranges of plasma creatinine and β_2 microglobulin of patients with normal plasma clearance of ^{51}Cr edetic acid are shown in table 1. Age had a greater effect on creatinine than β_2 microglobulin. Sex had no effect on the plasma β_2 microglobulin concentrations at

any age and the results of boys and girls were combined. A sex difference was observed between plasma creatinine concentration of boys and girls over 12 years.

Twenty two of the 80 observations showed abnormal clearance (range 10–77, mean (SD) 50 (25) ml/min/1.73 m²).

It has been suggested that the height:creatinine index can be used to predict glomerular filtration rate; and index of less than 1.5 corresponding to a glomerular filtration rate less than 80 ml/min/1.73 m² and greater than 2.1 predicting a glomerular filtration rate greater than 80 ml/min/1.73 m².²

Table 2 shows details of the results of the four tests considered. Plasma creatinine and β_2 microglobulin were considered abnormal if they were greater than the normal range in table 1. From these the sensitivities, specificities, and predictive values were calculated and are shown in table 3.

Table 2 Test results compared with plasma clearance of ^{51}Cr edetic acid

	Test result	Plasma clearance of ^{51}Cr edetic acid	
		>80 ml/min	<80 ml/min
β_2 microglobulin	–	57	7
	+	1	15
Creatinine	–	55	8
	+	3	14
Height:creatinine <2.1	–	46	2
	+	12	20
Height:creatinine	–	57	7
	+	1	15

Table 1 Plasma creatinine and β_2 microglobulin concentrations in children with a plasma clearance of ^{51}Cr edetic acid greater than 80 ml/min/1.73 m²

Age (years)	No of children		β_2 microglobulin (g/l)		Creatinine ($\mu\text{mol/l}$)	
	Boys	Girls	Geometrical mean	Range	Geometrical mean	Range
0.3–2.9	2	6	2415*	1306–4467	32.9*	15.0–73.0
3.0–7.9	8	6	2070	1462–2931	47.0*	34.9–63.2
8.0–11.9	9	9	1745	1067–2885	53.2	33.0–85.8
12+	12	6	1584	896–2802	58.8	39.5–87.4
Boys					66.0	44.3–98.2
Girls					48.0	42.0–54.9

*Significant difference from mean 12+ age group.

Table 3 Sensitivity, specificity, and predictive values of renal function tests. Results are percentages

Test	Sensitivity	Specificity	Predictive value of abnormal result	Predictive value of normal result
Creatinine >2 SD	64	95	82	87
β_2 microglobulin	68	98	94	89
Height:creatinine <2.1	91	79	63	96
Height:creatinine <1.5	68	98	94	89

Discussion

In a situation where no single test has clear advantages in terms of sensitivity and specificity, the relative importance of each must be considered. Table 3 shows that the sensitivity of height:creatinine index <2.1 is higher than the other tests but its specificity is inferior.

Failure to detect reduced glomerular filtration rate in a child could result in progression of disease, further deteriorating renal function, and irreversible damage. Conversely, the consequence of a false diagnosis of reduced glomerular filtration rate is that the patient will be referred for unnecessary additional investigations. A preliminary screening test must therefore, above all else, have a high sensitivity and a high predictive value of a normal test.

Plasma creatinine corrected for age and sex was more specific than height:creatinine index <2.1 but its sensitivity was inferior. Similarly, height:creatinine index <1.5 and β_2 microglobulin had high specificity but lower sensitivity. In addition, the higher cost and more complex assay procedure

required for β_2 microglobulin limit its usefulness as a screening test in routine clinical practise.

The test with clear advantages of higher sensitivity and higher predictive value of a normal result was height:creatinine index <2.1.

References

- 1 Payne RB. Creatinine clearance: a redundant clinical investigation. *Ann Clin Biochem* 1986;**23**:243–50.
- 2 Morris MC, Allanby CW, Toseland P, Haycock GB, Chantler C. Evaluation of a height/plasma creatinine formula in the measurement of glomerular filtration rate. *Arch Dis Child* 1982;**57**:611–5.
- 3 Wibell L, Evrin PE, Berggard I. Serum beta 2 microglobulin in renal disease. *Nephron* 1973;**10**:320–31.
- 4 Dubois D, Dubois EF. A formula to estimate the approximate surface area if height and weight be known. *Arch Intern Med* 1916;**17**:863–71.
- 5 Chantler C, Barratt TM. Estimation of glomerular filtration rate from plasma clearance of 51 chromium edetic acid. *Arch Dis Child* 1972;**47**:613–7.
- 6 Winberg J. The 24-hour true creatinine clearance in infants and children without renal disease. *Acta Paediatrica* 1959;**48**:443–52.

Correspondence to Dr A Parkin, Department of Medical Physics, St James's University Hospital, Beckett Street, Leeds LS9 7TF. Accepted 18 January 1989