Determination of glomerular function in advanced renal failure

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SUMMARY In 15 children with advanced chronic renal failure, glomerular filtration rate was determined by different methods. Inulin clearance correlated well with the mean of creatinine and urea clearance, and also with 51-chromium edetic acid (EDTA) clearance measured over 24 hours. The absolute values of creatinine clearance and of ^{51}Cr -EDTA clearance measured up to 8 hours were higher than inulin clearance. In advanced renal failure both the ^{51}Cr -EDTA clearance measured over 24 hours, and the mean of creatinine and urea clearance, provide acceptable estimates of true glomerular filtration rate.

The measurement of residual renal function is important in planning dialysis and transplant programmes, and serial measurements of glomerular filtration rate (GFR) are the most suitable method of predicting when dialysis will be required. Different methods of measuring GFR in advanced chronic renal failure have been compared in adults (Lubowitz *et al.*, 1967; Lavender *et al.*, 1969; Skov, 1970; Favre, 1973; Milutinovic *et al.*, 1975), but there are no comparable studies in children.

Patients and methods

Fifteen children, mean age 11 years (range 3-16), with advanced chronic renal failure were investigated; their diagnoses are shown in the Table. All children were in a stable condition at the time of the study. 4 were investigated twice. On the first day, GFR was determined by creatinine clearance (C_{CR}) and urea clearance (C_{urea}) with a 24-hour urine collection and a single serum specimen. The arithmetical mean of both clearance values (Lubowitz *et al.*, 1967) was also calculated. C_{CR} was also estimated from serum creatinine and body height (Counahan *et al.*, 1976).

On the second day a standard inulin clearance (C_{IN}) was performed with three collection periods (Stalder, 1960), each lasting for 20 minutes, and the single injection clearance of 51-chromium edetic acid (EDTA, Amersham) was determined. For the calculation of the EDTA clearances (C_{EDTA}) the radioactivity was measured in 10 serum specimens obtained 5, 10, 15, 30, 60, 90, 120, 180, 360, and 1440 minutes after injection of EDTA on the basis

of the two-compartment model of Sapirstein (Donath, 1971). The resolution of the plasma-disappearance curve was performed graphically in two different ways. Firstly, by using all sera up to 8 hours after injection ($C_{\text{EDTA}8}$), and secondly, by considering the serum specimens from 5 to 60 minutes and at 24 hours only ($C_{\text{EDTA}24}$). The only difference between the two procedures to calculate C_{EDTA} was a different half-life time of the latter part of the plasma disappearance curve.

Standard techniques were used for the analytical procedures (Richterich, 1968; Brodehl, 1969; Helger *et al.*, 1974) and for the evaluation of correlation coefficients (r). The calculation of the coefficient of variation of the three inulin clearance periods in each of the 15 patients was based on the logarithmic values (Zender *et al.*, 1968).

Results

The results obtained by the different methods for the evaluation of GFR are compared in the Table. C_{IN} ranged between 0.9 and 18.1 ml/min per 1.73 m^2 . The mean coefficient of variation of the three C_{IN} collection periods in each patient was 16%. Figs. 1, 2, and 3 compare the alternative methods of measuring GFR with C_{IN} . The correlation between C_{IN} and the reciprocal values of serum creatinine (S_{CR}) and serum urea (S_{urea}) was poor but improved when S_{CR} was corrected for height (Table) (Counahan *et al.*, 1976). The correlations to C_{CR} and to C_{urea} were good, but mean C_{CR} overestimated C_{IN} by 40%, whereas the mean C_{urea} was 22% less than C_{IN} . A high correlation as well as an acceptable agreement

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Table Determination of glomerular function in 15 children with advanced renal failure

Diagnosis	Height (cm)	C _{IN} (ml/min per 1.73 m ²)	S _{CR} (mg/100 ml)	$\frac{0.43 \times \text{height}}{S_{CR}}$	Clearances (ml/min per 1.73 m ²)				
					C _{CR}	C _{Urea}	$\frac{C_{CR} + C_{Urea}}{2}$	C _{EDTA8}	C _{EDTA24}
Oligomeganephronic hypoplasia	90)*	5.4	3.3	12.2	7.6	4.6	6.1	9.1	—
"	99)	5.7	4.8	9.3	9.6	3.5	6.5	6.5	5.6
"	140	4.2	14.8	4.2	3.9	3.0	3.5	5.5	3.6
"	124	5.3	6.5	8.6	7.3	5.4	6.4	7.6	5.5
"	130	12.0	4.9	11.9	14.8	9.8	12.3	10.9	10.0
Renal dysplasia	159	8.3	6.3	10.8	12.2	5.9	9.0	13.7	7.8
"	130	11.8	4.0	14.6	20.2	9.4	14.8	16.2	10.4
Nephronophthisis	121)	11.7	3.1	17.6	17.3	10.5	13.9	15.6	9.2
"	126)	9.4	7.2	7.9	8.6	6.4	7.5	7.5	7.1
"	148	7.7	5.6	11.9	10.2	7.0	8.6	9.6	6.6
"	148	7.0	6.7	9.9	14.3	6.9	10.6	8.5	6.8
"	150)	5.4	8.1	8.3	6.7	3.5	5.1	10.3	6.7
"	144	7.5	5.0	12.9	9.2	4.4	6.8	6.1	5.8
"	142	8.4	6.3	10.1	10.2	6.0	8.1	10.6	8.7
Chronic pyelonephritis	140	0.9	13.9	4.5	2.6	1.3	1.9	16.6	4.2
"	170	18.1	3.4	22.5	17.6	16.3	17.0	12.9	15.7
Endo- + extracapillary glomerulonephritis	149)	17.9	1.7	38.8	25.0	8.0	16.6	26.3	—
"	155)	6.9	3.8	18.3	18.5	9.1	13.8	10.9	9.2
Henoch-Schönlein nephritis	106	8.5	2.5	19.1	11.2	5.4	8.3	16.4†	16.7†
Mean		8.5		13.3	11.9	6.6	9.3	11.4	7.7
Coefficient of correlation (r) to C _{IN}			1/0.69	0.80	0.83	0.83	0.89	0.56	0.92

*Parenthesis indicates same patient investigated twice.

†This is the only patient with important proteinuria and overt oedema. These values are not included in calculation of the mean and r.

Conversion: Traditional units to SI—Serum creatinine: 1 mg/100 ml $\approx$ 88.4 μ mol/l. Fig. 1 Inulin clearance (C_{IN}) related to creatinine clearance and urea clearance.

with the mean value of C_{IN} (+9%), were obtained with (C_{CR} + C_{Urea})/2 (Fig. 2).

C_{EDTA8} did not significantly correlate with C_{IN} (P < 0.01), and overestimated it by 36%. On the other hand, C_{EDTA24} correlated well with C_{IN} (r = 0.92) and underestimated it by only 6%.

Fig. 2 Inulin clearance related to the mean of creatinine and urea clearance.

Discussion

It is generally accepted that while C_{IN} is the most accurate method of measuring GFR, even in advanced uraemia (Hierholzer *et al.*, 1972), it is not applicable to routine clinical practice (Barratt and Chantler, 1975). In adults the variation coefficient of C_{IN} in the same patient with normal or slightly impaired GFR varies between 8 and 12% (Zender *et al.*, 1968; Kramer *et al.*, 1974). In the present

Fig. 3 Inulin clearance related to 51-chromium edetic acid clearance (C_{EDTA}) measured up to 8 and 24 hours.

series of children with advanced chronic renal failure the variation coefficient was slightly higher.

C_{CR} overestimates GFR especially in chronic renal failure. This has been attributed to tubular secretion of creatinine, to fluctuations in the daily creatinine formation and excretion, and to interference of creatinine chromogenic material with the Jaffé reaction (Lubowitz *et al.*, 1967; Kim *et al.*, 1969; Hierholzer *et al.*, 1972). It has been known for a long time, that C_{Urea} underestimates GFR and is highly dependent on dietary protein intake. On the other hand, Lubowitz *et al.* (1967) showed in adults with advanced chronic renal failure that the mean of C_{CR} and C_{Urea} gives a good estimate of the true GFR. Our results show that the same applies to children with advanced chronic renal failure.

Recently isotopic single injection clearance techniques have become increasingly popular for the estimation of true GFR because of their simplicity, accuracy, and noninvasive nature. C_{EDTA} has been tested in large groups of children with normal or slightly impaired renal function (Vögeli *et al.*, 1971; Chantler and Barratt, 1972). Few data, however, have been published on the determination of GFR by C_{EDTA} in children with advanced chronic renal failure (Vögeli *et al.*, 1971). In adults with advanced chronic renal failure the single injection technique (C_{EDTA}) overestimates GFR (Favre, 1973). This has been attributed to an expansion of the extracellular volume, present even in the absence of overt oedema.

In newborn infants a similar mechanism seems to be responsible for the overestimation of GFR after feeding (Broberger, 1973).

The mathematical model used to analyse the falling plasma concentration curve is in any case an approximation and involves an overestimate of the plasma clearance of the chelate (Chantler *et al.*, 1969). This overestimate is small but becomes relatively more important when GFR is low and can be corrected for by extending plasma sampling (Maisey *et al.*, 1969).

Our study with $C_{\text{EDTA}24}$ suggests that in patients with advanced chronic renal failure one blood sample should be taken at 24 hours after injection to obtain an acceptable correlation with true GFR.

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