THREE HOUR CREATININE CLEARANCE TEST IN HEALTH AND DISEASE

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Summary: Endogenous creatinine clearance tests in which urine was collected for 3 and 24 hr on the same day were performed in 100 subjects. The control mean creatinine clearance by the 3 hr test was 99.2±23.7 (S.D.) *ml/min*/1.73 sq.m., in a group of 23 healthy subjects. The 3 hr creatinine clearance test was found to give a reliable index of renal dysfunction in 92 patients with minor or major renal dysfunction and has some advantages over the 24 hr test.

Key words: three and 24 hr creatinine clearance normal subjects renal disease

INTRODUCTION

In clinical practice, 24 hr endogenous creatinine clearance test is used as an index of glomerular function (1, 4, 5). However, complete collection of 24 hr urine, without loss of any portion is a problem for the "outpatients" and the "inpatients". Several investigators have reduced the period to overcome this difficulty (1,2,3). A very short collection period i.e. less than 60 min (1,2,3) may not conduce to complete voiding of the small volume of urine accumulated in the urinary bladder. A test period of 180 min would have two advantages; firstly the volume of urine collected would at least be 60 *ml* even in the presence of oliguria i.e. 24 hr urinary output of 500 *ml*. In addition, the collection of urine during this period could be closely supervised in the laboratory or out patients department. Therefore, we planned a prospective study to compare the results of creatinine clearance obtained at test periods of 3 and 24 hr.

MATERIALS AND METHODS

Creatinine clearance was measured in 100 subjects using two procedures i.e. test periods of 3 and 24 hr. The subjects were placed in 3 groups. Group A included 8 normal subjects. Group B included 58 patients with blood urea below 50 *mg%* (20 hypertensive patients; 11 patients of chronic pyelonephritis; 10 patients of diabetes mellitus; 2 patients of nephrotic syndrome and one each of polycystic kidney, horse-shoe kidney, motor neurone disease, coarctation of aorta and hypochromic anaemia). Group C included 34 uraemic patients with blood urea above 50 *mg%*

The two procedures were performed on the same day to exclude the role of change in the severity of the disease. The two procedures were performed in each subject thereby excluding the role of age and sex.

Serum creatinine was estimated by Broda's method and urinary creatinine was estimated by Bonsenes' method quoted by Varley (5).

In order to get reasonable control data for the 3 hr test period, the test was also performed in 15 additional normal subjects.

Details of procedures:

At 8.00 a.m. (zero hr), the subject was asked to void and discard the urine. The collection of urine for the 3 hr was thus started, and was completed at 11.00 a.m. If the period was not exactly 180 min the test period was recorded accurately in min. During the first half hr, 500 *ml* of water was given to promote water diuresis, which helped in a complete evacuation of the urinary bladder at the end of 3 hr. During the second hr venous blood was collected for estimation of serum creatinine and blood urea. The volume of urine collected during the test period was measured accurately in *ml* and its creatinine concentration was estimated.

The test was continued further beyond 11.00 a.m. upto 8.00 a.m. next morning. All the urine voided during this period (21 hr) and the last collection at 8.00 a.m. were pooled. The endpoint was timed accurately, to calculate the time period in min. This (21 hr) volume of urine was accurately measured, its creatinine concentration was estimated and creatinine excretion (21 hr) was calculated. The sum of creatinine excretinion in 3 and 21 hr gave 24 hr excretion.

Creatinine clearance was calculated as follows:

$$\text{Creatinine clearance} = \frac{\text{Urine creatinine } (mg) \text{ in 180 min (or 1440 min) x 100}}{\text{Serum creatinine } mg\% \text{ x180 (or 1440)}}$$

The value obtained was corrected for the standard surface area of 1.73 sq. m. as follows:

$$\frac{\text{Creatinine Clearance x 1.73}}{\text{Surface area of the subject}}$$

RESULTS

Table I gives the mean values ± S.D. of blood urea, serum creatinine and creatinine clearance.

TABLE I: Data on the blood urea, serum creatinine and creatinine clearance in normal subjects (Group A), subjects with minor renal dysfunction (Group B) and subjects with major renal dysfunction (Group C.)

Mean blood urea (*mg* ± *S.D.*)	*Mean serum creatinine* (*mg%* ± *S.D.*)	*Mean creatinine clearance* (*ml/min.*1.73 *sq.m* ± *S.D.*) 3 *hr*	24 *hr*	*P value*
Group				
A 16.1 ± 1.9	0.99 ± 0.19	94.6 ± 20.3	84.9 ± 23.5	>0.2
B 27.5 ± 9.6	1.2 ± 0.2	67.9 ± 30.4	55.6 ± 26.8	<0.05
C 130.3 ± 49.8	5.3 ± 4.1	23.2 ± 8.2	20.9 ± 18.8	>0.4
A vs B P<0.01	P<0.01	P<0.02	P<0.01	—
A vs C P<0.001	P<0.001	P<0.001	P<0.001	—

The mean 3 and 24 hr creatinine clearance values (*ml/min*/1.73 sq. m.) were 94.6 and 84.9 respectively in 8 normal subjects; the values in group B subjects were, 67.9 and 55.6 respectively and those in C group (uraemic) subjects were, 23.2 and 20.9 respectively.

The values obtained by the two procedures differed by 12%, 22% and 12% in groups A, B and C respectively. Only in patients of group B the difference between the procedures was statistically significant ($p<0.05$).

In 23 normal subjects the mean creatinine clearnace by the 3 hr test was 99.2±23.7 (range 70—137 *ml/min*/1.73 sq. m.).

DISCUSSION

Several tests for glomerular filtration are available. Inulin clearance is more precise than the urea and creatinine clearnace (5). However, intravenous infusion of inulin and catheterisation of urinary bladder are necessary. Thus the test is not suited for clinical practice. In healthy subjects, urea and creatinine clearances lag behind inulin clearance, but urea clearance is subject to wide variations. Therefore, creatinine clearnce test has been perferred by the clinicians. Tobias *et al.* (4) found that creatinine clearnace was more informative than any other single renal function test. Creatinine clearance test has been critically evaluated by Doolan *et al.* (1) and Kim *et al.* (2). They have confirmed the reliability and the value of serial repetitions of creatinine clearance for follow up and prognosis of renal disease. Creatinine clearance test has certain drawbacks e.g. wide normal range, diurnal variation, biological fluctuations, and the inclusion of chromogens within creatinine estimations. However, Tobias *et al.* (4) have reported that the estimation of true creatinine did not add to the reliability of the test. They also found that biological fluctuations disappear in the presence of renal disease. In renal disease simultaneous measurements of inulin and creatinine clearance showed that the disparity between them became less with rise in serum creatinine concentrations due to disease (1,4).

Our results have confirmed the reliability of both the procedures i.e. creatinine clearance at 3 and 24 hr.

Table I shows that there was significant urea and creatinine retention in group B patients and a significant reduction in the creatinine clearnce at both the time periods. Group B patients included patients, likely to have minor renal dysfunction. In group C patients, renal dysfunction was grossly reduced by all the criteria i.e. creatinine and urea retention and the creatinine clearance at the two time periods.

In all the three groups, the 3 hr creatinine clearance was higher than the 24 hr and was significant in patients of group B. This may be attributed to higher clearance during the day than during the night, or to a better collection of urine during 3 hr than during 24 hr. The higher 3 hr value should not be considered misleading, since in clinical practice the border-line patient would not be erroneously labelled as one of renal dysfunction on the basis of lower 24 hr value. Doolan *et al.* (1) reported that creatinine clearance in his one hr test was ten percent

higher than that during the 24 hr test. It is known that the 24 hr creatinine clearance lags behind inulin clearance in health and to a lesser extent in renal disease (1,4). Therefore, a higher value for the 3 hr test would tend to reduce the disparity between the inulin and creatinine clearances.

Our results also showed that creatinine clearances are probably lower in our population than in the western population. Doolan *et al.* (1) reported that the average normal 24 hr creatinine clearance rate (*ml/min*/1.73 sq. m.) was, 103 for males and 97 for females, confirming similar data reported by Tobias *et al.* (4). The average normal 24 hr creatinine clearance in our study was, 84. The reported average 1 hr creatinine clearance was, 115 (1). Our 3 hr value was 99 in 23 normal subjects. This difference may be attributed to our diet and our tropical climate.

The creatinine clearance rate for the three hr test ranged between 70 and 137 *ml/min/* 1.73 sq. m.; therefore we feel that values below 70 may be considered as subnormal.

Thus the 3 hr creatinine clearance test is reliable and we recommend its application routinely. It has additonal advantages. Doubtful results can be checked by reestimation. During follow up, the test can be easily repeated in the O.P.D. and hence may be useful in prognosis.

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