A Useful Method for Predicting Creatinine Clearance in Children

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A practical method for predicting creatinine clearance for pediatric patients from serum creatinine concentration and patient age is presented. Creatinine excretion rate (ER) can be predicted from the patient's age, in years, by the formula: ER = (0.035 × age) + 0.236. Using the predicted excretion rate and serum creatinine concentration, creatinine clearance can be predicted. There was good correlation (r = 0.90) between predicted and observed creatinine clearances in 101 subjects with various degrees of renal impairment. This method allows renal function to be rapidly estimated.

Additional Keyphrase: pediatric chemistry

Numerous studies have attempted to correlate creatinine clearance with factors such as age, weight, sex, and serum creatinine concentration in adult populations (1-4). There are, however, few such data for the pediatric population (5). The validity of estimating creatinine clearance from serum creatinine and other variables is particularly attractive in the pediatric population, for whom complete 24-h urine collections are difficult. Knowledge of the creatinine clearance significantly facilitates the adjustment of doses of medications that are primarily eliminated via the kidneys (6-8), and is essential for proper adjustment of fluid and electrolyte therapy. Here we report a method of predicting creatinine excretion rate (ER) and allowing for the prediction of creatinine clearance without the necessity of a 24-h urine collection.

Materials and Methods

Medical records at the Children's Hospital of Buffalo were screened for the period from January 1, 1974, to March 31, 1976. Data gathered included patient age, sex, height, weight, serum creatinine, and 24-h urinary creatinine excretion. Surface area was calculated by the method of DuBois and DuBois (9). Because creatinine excretion is a function of muscle mass and not adipose tissue, the weights of grossly obese patients were reduced to an average weight for that patient's height (10). This "lean" weight was then used to calculate "lean surface area." These data were collected on 46 male and 48 female patients ranging in age from 0.03 to 16.9 years, and were used to develop a creatinine excretion rate prediction method. Data from an additional 60 males and 41 females were collected for evaluation of the prediction method.

For development of the prediction method, creatinine concentration was determined manually by the alkaline picrate reaction after elution of creatinine from Lloyd's reagent (11). During evaluation of the prediction method, creatinine concentration was determined kinetically on the Rotochem IIA centrifugal analyzer (American Instrument Co., Division of Travenol Laboratories, Inc., Silver Springs, Md. 20910) (12).

Creatinine clearance values (ml/min per 1.73 m²) were obtained by using the following formula:

\[ \text{Creatinine clearance} = \frac{(\text{ER}) \times 100}{\text{serum creatinine}} \]  

where serum creatinine is in mg/dl and ER is the urinary excretion rate of creatinine (mg/min per 1.73 m²).

Results

Figure 1 depicts the relationship of urinary creatinine excretion rate to age in the 89 patients studied. The solid line is the linear regression line obtained by least-squares analysis. The broken lines indicate ±1 standard deviation about the regression line. Data for male and female subjects were also analyzed independently, but there was no significant difference between the slopes of the regression lines. The data were therefore pooled to generate the following regression equation:

\[ \text{ER} = (0.035 \times \text{age}) + 0.236 \]  

where ER is in mg/min per 1.73 m² and age is in years. This regression relationship was found to be highly significant: \( r = 0.64, P < 0.001 \).

With the above equation it is possible to predict a given ER by substituting the child's age in years and solving for ER. The resulting value may then be inserted into equation 1 to obtain an estimate of the creatinine clearance. This procedure was followed in the additional group of 101 patients. Figure 2 depicts the correlation of predicted and observed creatinine clearance values in these patients. A significant correlation was found to exist: \( r = 0.90 \).

Discussion

As is evident from Figure 1, there is much inter-subject variability in urinary excretion of creatinine at any given patient age. A similar observation has been made by Lewis et al. (13) in groups of subjects of similar heights. They report, for example, 24-h creatinine excretions ranging from 300 to 600 mg in patients 110 to 120 cm in height. Variability in muscle mass or incomplete urine collection, or both, could account for the observed variability in excretion rate. As evidenced by Figure 2, the use of mean data does allow for a reasonable prediction of creatinine clearance. This predictability would be expected to deteriorate in patients with an unusually large or small proportion of muscle tissue.

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The similarity of the slopes of the regression lines for the data on males and females is in agreement with the findings of Graystone (14). This author also reports that there was no significant difference between males and females in the slopes of the regression lines for creatinine coefficient (weight adjusted excretion rate) plotted against chronologic age. The difference between males and females in the percentage muscle composition of the body only begins to develop after 10 years of age (15). This observation explains why creatinine excretion rate, which is a function of muscle mass, should be similar for males and females until at least 10 years of age. From the years 10 to 16, boys develop a percentage muscle composition that exceeds by 50% that of girls (15). Thus, even though no significant difference in excretion rate could be found between males and females as a function of age, it is likely that the excretion rate for boys will be larger than the value for girls in the 10- to 16-year age group. Because of the large inter-subject variability, the exact magnitude of this difference could not be determined.

The data presented in Figure 2 demonstrate the accuracy of the proposed method in predicting creatinine clearance. This degree of accuracy was not anticipated, given the large degree of variability in the excretion rate data. The probable reason for the good overall predictability of the method is that serum creatinine plays a major role in the determination of the clearance. Changes in excretion rate as a function of age or due to inter-subject variability are relatively small (two- to threefold from the largest to the smallest values) compared to changes in serum creatinine resulting from renal impairment (5–100 mg/liter, or 20-fold). Thus, most change in creatinine clearance results from change in serum creatinine and is much less affected by changes in excretion rate.

It is important to compare predicted values to the normal creatinine clearance in children of the same age. Knowing the normal value for a given age will allow computation of the percent of normal renal function in a patient, given the predicted creatinine clearance. The data of Rubin et al. (16) have been summarized in Table 1 for use in estimating normal creatinine clearance in children of various ages. The data presented by these authors were on glomerular filtration rate, as estimated from mannitol clearance. In subjects with normal renal function, however, creatinine clearance only slightly exceeds glomerular filtration rate (17) and, in fact, the values are often used interchangeably. As may be seen from Table 1, glomerular filtration rate, when corrected for surface area of the child, markedly deviates from normal adult values only in children younger than one year. In this age group an estimated creatinine clearance of 50 ml/min per 1.73 m² of body surface would indicate normal renal function. In a child of two years, however, this estimate would indicate a 50% reduction in renal function.

Schwartz et al. (18) published a method for estimating creatinine clearance in which body length and serum creatinine concentration are used. These authors did not investigate the relationship of creatinine clearance to age. Their method of prediction (creatinine clearance = 0.55 × length in cm/serum creatinine in mg/dl) yielded an excellent correlation between predicted and observed values \( r = 0.955, n = 146 \). We plan prospective comparison of these two predictive methods.

We hope that the described method will allow the conversion of frequently available serum creatinine values into more meaningful estimates of renal function, i.e., creatinine clearance, and that these initial estimates will prove useful in patient care and drug therapy adjustment. It is not intended that these estimates of creatinine clearance replace the actual determination of this parameter. The estimated values should only serve as a guide to initial patient management while confirmation by standard techniques is awaited.

### Table 1. Normal Glomerular Filtration Rate (GFR) *

<table>
<thead>
<tr>
<th>Age</th>
<th>Mean</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;3 years</td>
<td>130</td>
<td>110–150</td>
</tr>
<tr>
<td>2 years</td>
<td>100</td>
<td>85–120</td>
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<tr>
<td>1 year</td>
<td>110</td>
<td>80–135</td>
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<tr>
<td>6–8 months</td>
<td>96</td>
<td>50–135</td>
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<tr>
<td>2–4 months</td>
<td>67</td>
<td>50–85</td>
</tr>
<tr>
<td>&lt;1 month</td>
<td>48</td>
<td>30–63</td>
</tr>
</tbody>
</table>

* Estimated from mannitol clearance (16).
References

10. Ibid., p 693.