Inulin and Creatinine Clearances in Children with Renal Disease

Lydia Kosnadi

(Department of Child Health, Medical School Diponegoro University, Kariadi Hospital, Semarang)

**ABSTRACT** To know how far the kidneys have been damaged, renal function in children suffering from renal disease must be measured. The aim of this study was to measure inulin and creatinine clearances in children suffering from renal diseases, and to know how would be the correlation between them. In this cross-sectional study sample size was estimated by the one-sample for estimating the population proportion, and data analysis was done by the Pearson product moment correlation and analysis of variance. Simultaneous measurements of inulin and creatinine clearance levels in 112 children were performed at Kariadi General Hospital, Telogorejo Hospital and St Elisabeth Hospital in Semarang, over the period from March 1991 to July 1993. Creatinine clearance ($C_c$) showed positive correlation with inulin clearance ($C_i$) in all patients with mixed (normal and decreased) renal functions: $C_c = 8.41 + 1.00 C_i$ ($r = 0.99; p < 0.001; n = 112$). Further it revealed that the difference between these two clearances was a function of the severity of the renal failure. These results were in accordance with those published in previous studies. [Paediatr Indones 1997; 37: 20-24]

**Introduction**

The importance of measuring or estimating of renal function or glomerular filtration rate (GFR) in children suffering from renal diseases is to know how far the kidneys have been damaged, as GFR is the aspect of renal function that correlates closely with the ability of the kidneys to maintain the composition of the body fluids within the ranges compatible with life. Three methods to measure GFR are $C_{in}$ (gold standard), radioisotope clearance ($C_{ra}$) (accurate) and $C_c$ (sufficiently accurate). There are
limitations for the utility of clearance methods. C_in takes a long time to perform, the procedure is difficult, very expensive, and is not practical for routine use in clinical practice. C_in is available only in a well-equipped and expensive health center. In clinical practice GFR is measured by endogenous C_cr. The advantages of knowing the level of GFR are the ability to detect the presence of decreased renal function, to know the severity of renal failure, to adjust drug and nutrient dosage on patients with decreased renal function, to know the results of treatment efforts, to follow the course of renal failure, and to prevent the progressivity of renal failure.

This study was performed since pediatric renal diseases in our country comprised about 2.3% of the hospitalized children, of which the frequency of renal failure was about 25%. Every child in the community could suffer from renal disease irrespective of their socioeconomic class, education, in urban or rural area. The aim of this study was to measure the levels of GFR, expressed by C_in and C_cr, in children suffering from renal diseases, and to know how would be the correlation between them.

Methods

The procedures of this study were in accord with the "Pedoman Etik Penelitian Kedokteran Indonesia", which is in accord with the ethical standards of the Committee on Human Experimentation in accord the Helsinki Declaration of 1975. This cross-sectional study was performed in children suffering from renal diseases, boys and girls, aged 2-14 years, admitted to the children ward of Kariadi General Hospital, Telogorejo Hospital, or St Elisabeth Hospital in Semarang. The sample size was estimated by the one-sample for estimating the population proportion seven. Measurements of the standard C_in and the conventional endogenous C_cr were undertaken simultaneously. A solution of 10% inulin as reagent was made by the method of CAS 9005-80-5.9 Inulin concentration in plasma (P_in)(mg/dl) and in urine (U_in)(mg/dl) were assayed by UV-method for D-fructose.10 Creatinine concentration in plasma (P_cr) and in urine (U_cr) were assayed by Abbott Spectrum Autoanalyzer. Urine flow was V ml per minute. Renal clearance formula of standard C_in is \[(U_in \times V) / P_in\] ml/min/1.73m² and that of conventional endogenous C_cr is \[(U_cr \times V) / P_cr\] ml/min/1.73m².4

To diagnose the status of renal function (normal or decreased), a standard renal function status test, namely IKA-1984, was utilized, based on the normal values for P_cr in children according to age and sex.11 The high clinical agreements (kappa >0.80) between IKA-1984 and other four standard renal function status tests, i.e., Schwartz,12 Feld,13 Barratt14 and Chantler,15 indicate that IKA-1984 method was accurate.16,17 Data were analyzed by the Pearson product moment correlation and the analysis of variance.18
Inulin and creatinine clearances in children with renal disease

Results

Simultaneous measurements of standard C_in and conventional endogenous C_er were performed in 112 children suffering from renal diseases, aged 2-14 years, consisted of 60 (60.9%) boys and 44 (39.1%) girls, over the period from March 1991 to July 1993 (29 months). The range of the standard C_in was from 3 to 177 ml/min/1.73m^2 and that of the conventional endogenous Ccr was from 4 to 196 ml/min/1.73m^2. Utilizing the IKA-1984 standard renal function status test revealed that there were 86 (76.7%) children with normal and 26 (23.3%) children with decreased renal function.

Creatinine clearance had positive correlation with C_in in 112 children with mixed renal functions (normal and decreased) showed by the regression equation as follows: Ccr = 8.41 + 1.00 Cto (r = 0.99; p < 0.001; n = 112). Further it was revealed that the difference between Ccr and C (ml/min/-1.73m^2) was a function of the severity of renal failure, the more severe the renal failure the more bigger the difference between C_cr and C_in (Table 1).

Table 1. Summary of analysis of variance

<table>
<thead>
<tr>
<th>Source of Variance</th>
<th>Sum of Squares</th>
<th>df</th>
<th>Mean square</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severity of renal failure</td>
<td>239.4</td>
<td>2</td>
<td>119.7</td>
<td>6.97</td>
<td>0</td>
</tr>
<tr>
<td>Residue</td>
<td>446.49</td>
<td>26</td>
<td>17.17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>685.89</td>
<td>28</td>
<td>24.49</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(Sum of squares for residue = sum of squares for total variation-sum of squares for within group variation)

Discussion

The results of this study showed that the levels of C_er were higher that those of C_in. This was in accord with those published by previous studies as follows:

1. Arant et al measured endogenous C_er and C_in simultaneously. It was shown that C_cr = 0.912 C_in + 9.51 (r = 0.94 and p < 0.001). At low levels of renal function the C_cr > C_in (GFR) by an average of 20%. Within normal and moderately reduced renal function the ratio of C_cr to C_in for practical purposes can be assumed to be unity.

2. Chantler and Holiday state when GFR is normal, tubular secreted is about 20% of the filtered creatinine, i.e. Ucr x V =120% filtered creatinine. As GFR declines, the percent of U_cr x V that is secreted rises in a variable way to an average of 160% of filtered creatinine when GFR is 40-80 ml/min/1.73m^2; it may reach values that are > 200% of filtered creatinine when GFR is < 40 ml/min/1.73 m^2. Consequently C_in as a measure of residual GFR tends to progressively overestimates GFR or Cin.

3. Hellerstein et al measured standard C_in and endogenous C_er simultaneously and
found a regression equation \( C_{in} = 0.86 \cdot C_{cr} - 6.5 \) \((r = 0.95)\).\(^{21}\)

4. Levery \textit{et al} stated an equation that showed the relationships between the sum of urine creatinine \((U_{cr} \times V)\), GFR, \(P_{cr}\) and sum of tubular secreted creatinine \((TS_{cr})\) was \(U_{cr} \times V = GFR \times P_{cr} + TS_{cr}\). Rearrangement of the above mentioned equation resulted in the next equation: \(C_{cr} = \frac{GFR \cdot TS_{cr}}{P_{cr}}\). Because \(C_{in} = GFR\), so it was proved that the level of \(C_{cr}\) was higher than that of \(C_{in}\).\(^{22}\)

Inulin clearance is accurate and \(C_{cr}\) is sufficiently accurate. Up till now in clinical practice the GFR is measured by \(C_{cr}\) because drug dosage adjusted on patients with decreased renal function is still expressed by \(C_{cr}\).

**Conclusions**

Positive correlation was observed between inulin and creatinine clearances performed in children with renal disease. The difference between them was a function of the severity of renal failure, the more severe the renal failure the bigger the difference.

**Acknowledgments**

The author wishes to extend her gratitude to Prof. Moeljono S Trastotenojo, MD, Prof. Imam Parsudi Abdulrochim, MD, PhD, Tonny Sadjimin, MD, PhD, Staffs and nurses of the Pediatric Department, Phapros Pharmaceutical Industry, Prodia Clinical Laboratory in Semarang, for their substantive contribution to this study.

**References**

Inulin and creatinine clearances in children with renal disease


