OXALIC ACID CONCENTRATION IN SERUM MEASURED BY ISOTOPIC CLEARANCE TECHNIQUE. EXPERIENCE IN HYPER- AND NORMO-OXALURIC SUBJECTS


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Summary

In a family from which two children suffered from primary hyperoxaluria the renal clearance of $^{14}$C oxalate was studied. The $^{14}$C oxalate/creatinine clearance ratio ranged from 1.76–2.63 (mean: 2.03) and appeared to be independent of glomerular filtration rate (GFR). The calculated plasma oxalate concentrations in normo-oxaluric subjects ranged from 0.1–0.9μmol/L, whereas in hyperoxaluric subjects values between 3.2–16.3μmol/L were found. The mean biological half-life of $^{14}$C oxalate was 2.7hr in subjects with normal renal function and increased proportionally with renal functional impairment. Recovery of $^{14}$C oxalate ranged from 87–112% (mean: 101%). All urine $^{14}$C activity was found in the oxalate fraction.

Introduction

Oxalic acid determination in serum by chemical methods in normal persons results in much higher values [1] than can be calculated from isotope-clearance studies [2–4]. We here report the results of clearance studies with $^{14}$C labelled oxalate in a family from which two children (C and E) suffered from primary hyperoxaluria. The clinical data of the family are given in Table I. Patient C had renal functional impairment, and was studied before as well as after oxalate excretion was decreased by vitamin B therapy and renal function improved. All other members, including child E, had normal renal function. The clearance study was not performed in the youngest child (F).

Methods

After an i.v. loading dose of 2μCi, a sustained-infusion of 2μCi $^{14}$C oxalate (specific activity 75mCi/mmol) was given over 4–6 hours. A constant level of $^{14}$C oxalate was only reached after two hours and could be maintained for
### TABLE I. Clinical Data of the Family

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age</th>
<th>Serum creatinine $\mu$mol/L</th>
<th>Glycolate creatinine mg/g</th>
<th>Urine Oxalate creatinine mg/g</th>
</tr>
</thead>
<tbody>
<tr>
<td>Father</td>
<td>died from lungcarcinoma</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mother (M)</td>
<td>45 years healthy</td>
<td>78</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>Children</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A ♂</td>
<td>9 months died from uraemia</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>B ♂</td>
<td>25 years healthy</td>
<td>98</td>
<td>12</td>
<td>5</td>
</tr>
<tr>
<td>C ♂</td>
<td>17 years renal oxalosis and stones</td>
<td>455</td>
<td>15</td>
<td>123</td>
</tr>
<tr>
<td>D ♀</td>
<td>15 years healthy</td>
<td>77</td>
<td>14</td>
<td>30</td>
</tr>
<tr>
<td>E ♀</td>
<td>13 years healthy</td>
<td>66</td>
<td>54</td>
<td>106</td>
</tr>
<tr>
<td>F ♀</td>
<td>10 years healthy</td>
<td>64</td>
<td>9</td>
<td>26</td>
</tr>
</tbody>
</table>

Two to four hours thereafter. An indwelling catheter was inserted at the beginning and adequate diuresis was ensured by drinking 1.5L water during the study. Plasma and urine samples were taken during two to four successive periods, from which the $(^{14}C)$ oxalate clearance ($C_{ox}$) was calculated. The mean 24 hour oxalate excretion (modified Archer method [5, 6]) and creatinine clearance during the three preceding days was also determined. The plasma oxalate concentration was calculated from the formula:

$$P_{ox} = \frac{\text{oxalate excretion (chemical) per minute}}{C_{ox} \text{(isotopic)}}$$

![Cumulative $^{14}C$ oxalate urine excretion and subsequent $t_{1/2}$, Subject C*](image-url)

Figure 1. Cumulative $^{14}C$ oxalate urine excretion and subsequent $t_{1/2}$, Subject C*
After stopping the \((^{14}C)\) oxalate infusion the biological half-life of the radiopharmaceutical could be determined (Figure 1). In addition the recovery of \((^{14}C)\) oxalate could be determined by means of the cumulative excretion in the urine.

**Results**

The \(C_{OX}/C_{Creat}\) ratio appeared to be ± 2.0, independent of the glomerular filtration rate (Table II). The \(P_{OX}\) for persons with a normal oxalate excretion varied from 0.1–0.9 \(\mu\)mol/L, a value ± 10 times lower than the lowest values reported with chemical methods and ± 2 times lower than the values reported by Williams

<table>
<thead>
<tr>
<th>Subject</th>
<th>Clearance ml/min ((^{14}C)) oxalate creatinine</th>
<th>(C(^{14}C)) oxalate (C) creatinine</th>
<th>plasma oxalate concentration (\mu)mole/L</th>
<th>recovery %</th>
<th>T(\frac{1}{2}) hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>175</td>
<td>78</td>
<td>2.24</td>
<td>0.9</td>
<td>98</td>
</tr>
<tr>
<td>B</td>
<td>246</td>
<td>140</td>
<td>1.76</td>
<td>0.1</td>
<td>111</td>
</tr>
<tr>
<td>C*</td>
<td>47</td>
<td>25</td>
<td>1.88</td>
<td>16.3</td>
<td>87</td>
</tr>
<tr>
<td>C**</td>
<td>77</td>
<td>41</td>
<td>1.88</td>
<td>5.1</td>
<td>92</td>
</tr>
<tr>
<td>D</td>
<td>279</td>
<td>106</td>
<td>2.63</td>
<td>0.9</td>
<td>106</td>
</tr>
<tr>
<td>E</td>
<td>209</td>
<td>117</td>
<td>1.79</td>
<td>3.2</td>
<td>112</td>
</tr>
</tbody>
</table>

\(C^*\) before and \(C^{**}\) after vitamin B therapy

\(T\frac{1}{2}\) biological half-life

[2], Pinto [3] and Constable [4]. In patient E, with hyperoxaluria and hyperglycolic aciduria, but normal renal function, \(P_{OX}\) was already substantially elevated. In patient C, who after therapy showed both a decrease in oxalate excretion and a rise in \(C_{Creat}\), \(C_{OX}\) increased to the same degree. The biological half-life showed an inverse relation with \(C_{OX}\). The mean recovery of \((^{14}C)\) oxalate in the urine was 101%. All urine \((^{14}C)\) activity was found in the oxalate fraction (Table II).

**Conclusions**

Plasma oxalate levels can be safely and accurately measured by the isotopic technique. Chemical methods are inadequate to measure serum oxalate concentrations in normal persons as well as in hyperoxaluric patients with normal or slightly impaired renal function. Oxalate clearance exceeds glomerular filtration rate by a fairly constant factor irrespective of the renal functional impairment.

**Acknowledgments**

This research was supported by a grant from the Dutch Kidney Foundation.
References


Open Discussion

WILL (Nottingham) What dose of pyridoxine was used and what preparation of it?

PRENEN We give as therapy, initially, to our patients 100mg pyridoxine and 200mg thiamine.

WILL Have you tried any higher dosages in your patient who was not actually normalised?

PRENEN Patient E we treated with thiamine, and the oxalate excretion in urine was reduced more than half. Her excretion is now about the high limit of normal.

WILL Are repeated readings stable, because oxalate excretion seems to vary very much from day to day.

PRENEN I think the excretion of oxalate is rather stable, when you collect for 24 hours accurately.

WILL There might be some debate on that question. Can I ask a second question? Were there any abnormalities of urinary calcium excretion or acid/base handling in the asymptomatic relative with hyperoxaluria?

PRENEN We only studied these two patients and we found no further abnormalities.

BIJVOET (Chairman) You make a pronouncement about the serum oxalate concentration and your pronouncement is based on a calculation using also a urinary oxalate determination. Now, why is the value you derive from the isotopic method lower than other isotopic methods in the literature, and how did you check the accuracy of your urinary oxalate determination? Because of course determination of oxalate in the urine is also a difficult method.

PRENEN The urine oxalate was determined for the three preceding days and we took the mean of it.

BIJVOET Yes, but what method did you use?

PRENEN A modified Archer method. In the family members with normal
oxalate excretion in the urine the values ranged between 5 and 35mg/24hr. These values are in good agreement with the normal values of other authors.

BIJVOET What kind of method is that?

PRENEN That is a precipitation and titration method.

BIJVOET So if you have an incomplete recovery, and you get it readily with a precipitation method, you would have too low a serum oxalate, so how are you sure that you were not in error, because this is the sensitive point.

PRENEN I think by the method we used we have precipitated all the oxalate.

BIJVOET Well, you hope!