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References

Multiple Overnight Urine Collections May Be Used for Estimating the Excretion of Electrolytes and Creatinine

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We studied the excretion of sodium, potassium, calcium, magnesium, and creatinine in overnight and 24-h urines collected over a period of seven consecutive days from 28 Dutch boys, ages eight and nine years. The correlation coefficients for the relation between true mean overnight and true mean 24-h excretion ranged between 0.94 and 1.00 for sodium, calcium, magnesium, and creatinine and was equal to 0.61 for potassium. Generally the within-person coefficients of variation for overnight excretions (range, 33–52%) were greater than for 24-h excretions (range 16–35%). We conclude that overnight collections may replace 24-h collections in the case of young boys, but that generally more overnight than 24-h urine specimens are required to achieve a similar degree of precision. The exact number of urine specimens required varies with the aims of the study.

Additional Keyphrases: salt intake and blood pressure • hypertension • creatinine • sodium, potassium, magnesium, calcium excretion • pediatric chemistry

In comparisons between populations, sodium intake has been found to be positively correlated with blood pressure (1, 2). However, studies within populations have given inconsistent results. In some studies a positive correlation was found (3); in others, none (4–6). Various explanations have been given for the absence of a positive relationship between salt intake and blood pressure within populations, including the role of within-person variation (7). In many studies only one 24-h urine specimen is being collected from each subject, and blood pressure is only measured once. But day-to-day variations in sodium excretion and blood pressure may be large, and this may obscure the relationship between salt intake and blood pressure. Also, most studies in which hypertensive patients were compared with normotensive people have not shown a difference in sodium excretion between hypertensives and normotensives (8). An unfavorable ratio of within-to-between-person variance, which may lead to considerable misclassification of subjects with respect to blood pressure and sodium excretion, may be at least partly responsible for this.

To diminish the role of within-person variation in sodium excretion, one may collect more than one 24-h urine specimen from each subject participating in studies of the salt–blood pressure relationship. Collection of multiple 24-h urine specimens, however, is a tremendous task for epidemiological studies of free-living populations. Overnight urine specimens are much easier to collect, and true (i.e., habitual or baseline) mean overnight sodium excretion correlates reasonably well with true mean 24-h sodium excretion (9, 10).

In this study we have investigated the degree of consistency between values for repeated overnight and repeated 24-h excretion of sodium, potassium, calcium, magnesium, and creatinine by 28 Dutch boys, ages eight and nine years.

Methods

Subjects. In 1985, the heads of six randomly selected primary schools in Wageningen, a college town of 30 000 inhabitants in the central part of the Netherlands, were informed of the aim and design of the study. Four schoolheads responded positively to our invitation to participate in the study, and all 36 boys of ages eight and nine years from the four schools received a letter for their parents. In this letter the parents were told about the aims of the study and what was expected of the boys and their parents if they would decide to participate in the study. The parents were also asked to give permission for their son to participate in the study. Finally, 28 boys (78%) and their parents agreed to participate.

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Collection of urine. Urine was collected for seven consecutive days. For each day, three containers, each containing 250 mg of thymol as preservative, were provided for the daytime, evening, and overnight urine specimens. The "daytime" collection started after the subject had arisen and passed the first urine into the overnight collection container, and continued until supper. The "evening" collection began at supper and ended with going to bed. The overnight collection included any urine voided at night and the first urine voided the following morning.

Before the urine collection was started, each boy was instructed individually on how to collect urine during a home visit made by one of us (GvP). During this visit the boy was provided with labeled containers, a bag in which to carry the containers, and a booklet with clear instructions and funny illustrations on the collection of urine. In this booklet the boy could write down the times for getting, having supper, and going to bed, the number of times he missed voiding into the collecting container, and also his estimate of the amount of urine that got lost each time.

The containers were collected each day and three new containers were provided during a home visit in the evening. The boy was then also queried on the completeness of his collection, and the notes in his booklet were checked against oral information from the parents and the boy himself. During this interview, which was always held in a relaxed atmosphere, it was emphasized that it was more important to report on possibly incomplete collections than to deliver a complete collection.

Laboratory procedures. Immediately after collection the urine specimen was weighed, 3 mL of glacial acetic acid was added, and the specimen was thoroughly mixed. Aliquots were then taken and stored at -20 °C until analysis, which was carried out within two months.

After diluting the urine with a 1 g/L solution of Ca^{2+}, sodium and potassium were measured by flame atomic absorption spectrophotometry (Model 2380, Perkin Elmer) with aqueous calibration standards. Calcium and magnesium were measured in a similar way after diluting the urine with a 6 g/L solution of La^{3+}. Creatinine was measured by the method of Jaffe, with alkaline picrate, in an Abbott ABA 200 bichromatic analyzer (11).

Statistical methods. Only those urine collections reported as complete were used in the analysis.

Group means were calculated by estimating the mean for each subject, followed by calculating the (non-weighted) average of these means. Coefficients of variation were calculated from analysis of variance with logarithmically transformed data, as this is the appropriate way of modeling proportionality between within-person variation and the individual mean value (12).

As an illustration of the use of within-person variance values, we calculated the number of measurements (k) needed to estimate the individual excretion of different electrolytes and creatinine within 20% of a person's habitual excretion (95% confidence interval) ranged between three for the 24-h creatinine excretion and 26 for the overnight calcium excretion (Table 1).

Table 2 gives the weighted averages of the sample correlation coefficients between overnight and 24-h excretions of the electrolytes and creatinine. These correlations ranged between 0.15 for potassium and 0.64 for calcium. The estimated coefficients of correlation between the true mean 24-h and overnight excretion of electrolytes and creatinine were close to 1, except for that for the relation between the true mean 24-h and overnight excretion of potassium (0.61), which may be related to the relatively low proportion of potassium that is excreted during the night (Table 2).

Table 3 gives the ratios of within- to between-person variance for the 24-h and overnight excretions of electrolytes and creatinine. The ratio of within- to between-person variance was low for the 24-h excretion of calcium (0.3) and magnesium (0.8) and also for the overnight excretion of calcium (0.7), but it was high for the 24-h excretion of sodium (3.1) and the overnight excretions of potassium,
Table 1. Mean Values, Within- and Between-Person CVs for Excretion of Electrolytes and Creatinine, and Number of Urine Collections (k) Required*

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Mean, mmol</th>
<th>Within-person</th>
<th>Between-person</th>
<th>k*</th>
</tr>
</thead>
<tbody>
<tr>
<td>24-h sodium</td>
<td>101</td>
<td>35</td>
<td>20</td>
<td>12</td>
</tr>
<tr>
<td>Overnight sodium</td>
<td>34</td>
<td>48</td>
<td>32</td>
<td>22</td>
</tr>
<tr>
<td>24-h potassium</td>
<td>47</td>
<td>28</td>
<td>19</td>
<td>8</td>
</tr>
<tr>
<td>Overnight potassium</td>
<td>13</td>
<td>44</td>
<td>22</td>
<td>19</td>
</tr>
<tr>
<td>24-h calcium</td>
<td>2.3</td>
<td>35</td>
<td>60</td>
<td>12</td>
</tr>
<tr>
<td>Overnight calcium</td>
<td>1.0</td>
<td>52</td>
<td>61</td>
<td>26</td>
</tr>
<tr>
<td>24-h magnesium</td>
<td>3.6</td>
<td>22</td>
<td>24</td>
<td>5</td>
</tr>
<tr>
<td>Overnight magnesium</td>
<td>1.9</td>
<td>40</td>
<td>22</td>
<td>18</td>
</tr>
<tr>
<td>24-h creatinine</td>
<td>5.5</td>
<td>16</td>
<td>16</td>
<td>3</td>
</tr>
<tr>
<td>Overnight creatinine</td>
<td>2.4</td>
<td>33</td>
<td>16</td>
<td>11</td>
</tr>
</tbody>
</table>

*To estimate the excretion of electrolytes and creatinine to within 20% of the habitual excretion (95% confidence interval) assuming constant within-person CV.

b See equation 1.

Table 2. Estimated Correlation Coefficients for the Relation between Excretion of Electrolytes and Creatinine in an Overnight Portion on One Day with That in a 24-h Portion on Another Day

<table>
<thead>
<tr>
<th>Analyte</th>
<th>ρ(C1, C2 + D)</th>
<th>ρ(X, X + Y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>0.26</td>
<td>0.95</td>
</tr>
<tr>
<td>Potassium</td>
<td>0.15</td>
<td>0.61</td>
</tr>
<tr>
<td>Calcium</td>
<td>0.64</td>
<td>0.94</td>
</tr>
<tr>
<td>Magnesium</td>
<td>0.41</td>
<td>1.00</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.35</td>
<td>1.00</td>
</tr>
</tbody>
</table>

a ρ(C1, C2 + D) and of the true mean overnight excretion with the true mean 24-h excretion, i.e., ρ(X, X + Y).

b The estimate of the true correlation coefficient slightly exceeded 1. As the true correlation coefficient cannot exceed 1, 1.00 is given as the best estimate.

Table 3. Variance Ratios for the Excretion of Electrolytes and Creatinine, and Number of Samples Required to Decrease the Resulting Diminution of the Correlation Coefficient Involving the Overnight (k0) or 24-h (k) Excretion of Electrolytes or Creatinine to 10% of the True Value

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Overnight</th>
<th>24-h</th>
<th>k0</th>
<th>k</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>2.3</td>
<td>3.1</td>
<td>10</td>
<td>14</td>
</tr>
<tr>
<td>Potassium</td>
<td>4.0</td>
<td>2.2</td>
<td>17</td>
<td>10</td>
</tr>
<tr>
<td>Calcium</td>
<td>0.7</td>
<td>0.3</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Magnesium</td>
<td>3.3</td>
<td>0.8</td>
<td>14</td>
<td>4</td>
</tr>
<tr>
<td>Creatinine</td>
<td>4.3</td>
<td>1.0</td>
<td>18</td>
<td>5</td>
</tr>
</tbody>
</table>

magnesium, and creatinine (3.3–4.3). Using equation 3, we calculated the number of samples required to reduce the resulting diminution of the correlation coefficient involving the overnight excretion of electrolytes or creatinine to 10% of the true value as the minimum value of k for which the ratio ρ(Ck, X + Y)/ρ(X, X + Y) was at least 0.90 (Table 3). The same applies to the 24-h excretion, using equation 4 and the ratio ρ(Ck + D, Ck + D, X + Y)/1. This number was small (<5) for both the overnight and 24-h excretion of calcium and also for the 24-h excretion of magnesium, while it was high (>13) for the overnight excretions of potassium, magnesium, and creatinine, and also for the 24-h excretion of sodium.

The expected value for the apparent coefficient of correlation between the mean overnight or 24-h excretion and the true 24-h excretion depends on the number of collections per person (Figure 1). It can be seen from the curves that the effect of increasing the number of collections on decreasing the diminution of the apparent correlation coefficient becomes less and less as the number of collections increases. The exact shape of the curve depends also on the ratio of within- to between-person variance (Table 3). For example, for calcium, with a low ratio of within- to between-person variance, there is not much sense in making a large number of collections, while the opposite is true for overnight creatinine, which has a high ratio of within- to between-person variance. It should be noted, however, that the values for the apparent correlation coefficients can only approximate those for the true correlation coefficients by increasing the number of collections, but that they can never exceed the values for the true correlation coefficients.

Discussion

The within-person CVs for the 24-h excretions of sodium, potassium, and calcium are basically similar to those reported for adults in our previous study (13), but those for magnesium and creatinine are considerably lower. The ratios of within- to between-person variance for the overnight and 24-h excretion of sodium differ somewhat from the data (2.3 compared with 2.6 for overnight and 3.1 compared with 2.2 for 24-h sodium excretion) of Liu et al. (10) for boys six to 10 years old.

correlation coefficient
The answer to the question of whether overnight urine collections can validly replace 24-h urine collections depends on the aims of the study and on the degree of consistency between overnight and 24-h urine collections. For creatinine and the electrolytes, except for potassium, there is a good degree of consistency between true mean overnight and true mean 24-h excretion. Thus, regarding degree of consistency, overnight urine collections can replace 24-h urine collections for the estimation of creatinine and electrolytes, except for potassium. Thus, no practical advantage would be realized by substituting overnight for 24-h collections if one intends to measure potassium excretion accurately.

The clinical chemist is probably most often interested in someone's baseline excretion of a particular electrolyte. The precise number of collections required for this purpose is determined by the within-person variance. We have shown (Table 1) that the number of overnight collections required is two to four times greater than the number of 24-h collections when someone's excretion is to be estimated to within 20% of the baseline excretion. However, it is more convenient to collect overnight samples than 24-h specimens.

In correlation analysis, not only the within-person variance but rather the ratio of within- to between-person variance is important, because this ratio determines the diminution of the true correlation coefficient. Owing to the relatively great differences in true mean, overnight calcium excretion has a favorable ratio of within- to between-person variance and therefore, only three overnight urine specimens per subject would suffice to decrease the resulting diminution of the correlation coefficient to 10% of the true value. This is clearly in contrast to the number of samples required for the correct classification of subjects with respect to overnight calcium excretion, for which as many as 26 samples (Table 1) would be required.

Besides the precision of the estimate, its validity also should be taken into account. From that point of view, for example, the estimate of true mean potassium excretion based on 17 overnight collections is less valid than that based on 10 24-h excretions. The corresponding correlation coefficients of the mean values with true mean 24-h potassium excretion are 0.55 for the overnight, 0.91 for the 24-h excretions.

In this study we have shown that there is generally a good degree of consistency between true mean values for overnight and true mean values for 24-h excretion of electrolytes and creatinine—i.e., the mean value for habitual or baseline specimens. However, the within-person variance and also the ratio of within- to between-person variances are generally larger for overnight than for 24-h excretions. Therefore, we conclude that overnight collections may replace 24-h collections in young boys, but that, in general, more overnight than 24-h urine samples are required to obtain a similar degree of precision. Although there is the disadvantage of collecting more overnight than 24-h specimens, it is probably much more convenient to most people to collect overnight specimens.

Whether the results of this study in children can be extrapolated to adults and, more generally, to other populations remains to be investigated.

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References