Endourology and Stones

Twenty-four Hour and Spot Urine Metabolic Evaluations: Correlations Versus Agreements

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OBJECTIVES
To investigate the correlations and agreements between the solute/creatinine ratios from the 24-hour and early morning spot urine samples for metabolic evaluation in stone-formers given the various pitfalls with the 24-hour urinary metabolic evaluation in stone-formers.

METHODS
30 urinary stone-formers out of an initial 62 recruited provided a complete 24-hour urine and early morning spot urine samples for metabolic evaluation. Pearson correlation and Bland and Altman Test were used to assess the correlations and agreements.

RESULTS
Significant correlations were established between the 24-hour urinary solute excretions and the corresponding early morning spot urine solute/creatinine ratios for calcium, magnesium, urate, potassium, oxalate, citrate, and the Differential Gibb’s free energy value of calcium oxalate DG(CaOx) values. However, all these solute/creatinine measurements between the 24-hour and early morning spot urine samples were judged to be not within the acceptable limits based on the estimated “limit of agreement” by the Bland and Altman Test of Agreement. Diurnal circadian rhythm and postprandial excretion surge are thought to be responsible for the disagreements.

CONCLUSIONS
Thus, the early morning spot urine is not suitable to be used interchangeably to replace the 24-hour urine collection in the evaluation of urinary metabolic abnormalities in stone-formers. A good correlation does not translate to an agreement between the 2 measurements. UROLOGY 75: 1294–1298, 2010. © 2010 Elsevier Inc.

The value of urinary metabolic evaluation in the prevention of urinary stone recurrence cannot be further emphasized. It has generally been regarded as part of the optimal management of urinary stone patients. To date, 24-hour urine collection has been the gold standard for metabolic evaluation in urinary stone disease. However, it is a very tedious, time-consuming, and high commitment-requiring procedure that is deemed to be unsuitable for working patients who constitute a big proportion of the stone-formers. Though, the motivation of patients in collecting a 24-hour urine sample was shown to be good, their motivation was decreased when more than one 24-hour urine samples were required (94% vs 79%). The practice of 24-hour urine collection is further complicated by the fact that the adequacy of a single 24-hour urine collection for evaluating the risk of stone formation is still debatable. To our naïveté, collection of urine at the workplace or public places in certain societies is regarded as socially unacceptable. Therein, a simpler and comparable urinary metabolic evaluation method for stone-formers is much needed.

Several studies have assessed the prospect of using spot urine or timed, urine samples for metabolic evaluation. As the glomerular filtration rate and creatinine excretion rate are fairly constant over a 24-hour duration, significant correlations between the 24-hour urine calcium and phosphate excretions and their corresponding spot urine calcium/creatinine and phosphate/creatinine ratios were demonstrated in the urinary metabolic evaluation of stone-formers. Correcting the urinary solutes concentration with creatinine value would eliminate the effect of volume variations, thus providing a solute/creatinine ratio, which corresponds to the 24-hour solute excretion. The low compliance and inadequate collection of 24-hour urine samples can give rise to invalid results and wastage of valuable resources in healthcare. With this in mind, a study was carried out to assess the validity of early morning spot urine solute/creatinine ratio to replace the 24-hour urine analysis.

PATIENTS AND METHODS
Urinary stone-formers attending the urology clinic at the University of Malaya Medical Center (UMMC) were requested to provide an early morning urine sample followed by a 24-hour urine sample on their habitual and self-selected diet on a voluntary basis (as urinary metabolic evaluation was not a routine procedure). Stone-formers with difficulties in mobility...
or urine collection, diagnosed with hypercalcemia or hyperparathyroidism were excluded. Only those who provided a complete 24-hour urine sample defined as urinary creatinine/H110630% of the idealized creatinine (22.1 mg/kg in men and 17.2 mg/kg in women)13 during the study period were included. The study protocol was approved by the Medical Ethics Committee, UMMC (reference number 571.11).

The early morning spot urine and the 24-hour urine samples were collected into separate plain plastic containers. Post-delivery acidification (pH/H110212.0) was done to an aliquot from each sample immediately after delivery to the laboratory.14 The acidified aliquots were used to determine the urinary calcium, phosphate, magnesium, oxalate, and citrate, whereas creatinine, sodium, potassium, and urate were assayed from the untreated aliquots. Urinary calcium, magnesium, phosphate, creatinine, sodium, potassium, and uric acid concentrations were assayed by Clinical Diagnostic Laboratory, UMMC using Dimension Clinical Chemistry System and QuikLYTE Integrated Multi-sensor according to their routine protocols. A small aliquot of acidified urine sample was frozen at −80°C for the determination of urinary oxalic and citric acids. The assay was carried out at the SUXCeS Laboratory, Department of Pharmacology, Faculty of Medicine, University of Malaya using the newly developed and validated Reverse-Phase high performance liquid chromatography method (interassay coefficient of variation was 6.5% and the intraassay was 4.0%). The Differential Gibb’s free energy value of calcium oxalate [DG(CaOx)] was used to estimate the urinary saturation level.5

### Statistical Analysis

The correlation between the 2 variables was determined by Pearson correlation using statistical software—SPSS version 13. The significance level was set at P <.05. Bland and Altman Test of Agreement plot on assessing the agreement between the solute/creatinine ratios from the 24-hour and early morning spot urine samples.

### RESULTS

62 stone formers initially consented to participate in the study from all those approached during the study period. Slightly more than 30% of the consented stone-formers failed to provide urine samples for various reasons. Approximately 28% of those who provided 24-hour urine samples failed to collect their urine completely. Hence, only about 48% of the stone-formers provided a meaningful 24-hour urine sample for metabolic evaluation. The correlations between the 24-hour urinary solute excretions and their corresponding early morning spot urine solute/creatinine ratios are presented in Table 1. Urinary calcium, magnesium, urate, potassium, oxalate, and citrate, and DG(CaOx) values demonstrated significant correlations between the 24-hour and early morning spot urine measurements in which citrate and DG(CaOx) showed a strong correlation (r = .8).

The Bland and Altman Test of Agreement plot on assessing the agreement between the 24-hour and early morning spot urine DG(CaOx) is shown in Figure 1. The “limit of agreements” and mean differences from the Bland and Altman Test of Agreement for various individual urinary solute/creatinine ratios and the urinary saturation [DG(CaOx)] between the 24-hour and early morning spot urine samples are summarized in Table 2. The 24-hour urinary solute/creatinine ratios for the calcium, phosphate, magnesium, sodium, oxalate, and citrate as well as the DG(CaOx) value were judged to be not in agreement with their corresponding measurements from the early morning spot urine samples due to the clinically significant range of variation of the “limit of agreement.”

### COMMENT

In contrast to the previously reported good motivation in the 24-hour urine collection procedure among the stone-
Table 2. Limit of agreements and mean differences of 24-hour and early morning spot urine solute/creatinine ratios with their respective mean, 25th percentile, median and 75th percentile values from the early morning spot urine of stone-formers (n = 30)

<table>
<thead>
<tr>
<th>Solute/Creatinine Ratio</th>
<th>Limit of Agreement</th>
<th>Mean Difference (Confidence Interval)</th>
<th>Normal Solute/Creatinine Ratio*</th>
<th>Range</th>
<th>25th Percentile</th>
<th>50th Percentile</th>
<th>75th Percentile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium/creatinine</td>
<td>-0.381 to 0.247</td>
<td>-0.067 (CI -0.126 to -0.008)</td>
<td>&lt;0.6</td>
<td>0.0721-1.0822</td>
<td>0.2373</td>
<td>0.4134</td>
<td>0.7238</td>
</tr>
<tr>
<td>Phosphate/creatinine</td>
<td>-1.004 to 0.514</td>
<td>-0.245 (CI -0.387 to -0.103)</td>
<td>&lt;2.7</td>
<td>1.40-3.54</td>
<td>1.8525</td>
<td>2.1599</td>
<td>2.5876</td>
</tr>
<tr>
<td>Magnesium/creatinine</td>
<td>-0.259 to 0.149</td>
<td>-0.055 (CI -0.093 to -0.017)</td>
<td>&gt;0.2</td>
<td>0.1081-0.6667</td>
<td>0.2353</td>
<td>0.3636</td>
<td>0.4408</td>
</tr>
<tr>
<td>Urate/creatinine</td>
<td>-0.130 to 0.131</td>
<td>0.001 (CI -0.024 to 0.025)</td>
<td>NA</td>
<td>0.17-0.52</td>
<td>0.2370</td>
<td>0.3078</td>
<td>0.4118</td>
</tr>
<tr>
<td>Sodium/creatinine</td>
<td>-20.813 to 15.709</td>
<td>-2.552 (CI -5.962 to 0.857)</td>
<td>&lt;28</td>
<td>4.17-39.52</td>
<td>8.8033</td>
<td>15.2992</td>
<td>25.0054</td>
</tr>
<tr>
<td>Potassium/creatinine</td>
<td>-4.135 to 4.237</td>
<td>0.051 (CI -0.731 to 0.832)</td>
<td>NA</td>
<td>1.25-13.07</td>
<td>1.9303</td>
<td>3.0487</td>
<td>3.7782</td>
</tr>
<tr>
<td>Oxalate/creatinine</td>
<td>-0.034 to 0.028</td>
<td>0.000 (CI -0.009 to 0.003)</td>
<td>&lt;0.03</td>
<td>0.0131-0.0978</td>
<td>0.0298</td>
<td>0.0416</td>
<td>0.0513</td>
</tr>
<tr>
<td>Citrate/creatinine</td>
<td>-0.110 to 0.148</td>
<td>0.019 (CI -0.005 to 0.043)</td>
<td>&gt;0.2</td>
<td>0.0113-0.4055</td>
<td>0.0440</td>
<td>0.0887</td>
<td>0.1560</td>
</tr>
<tr>
<td>DG(CaOx)</td>
<td>-1.274 to 0.704</td>
<td>-0.285 (CI -0.470 to -0.100)</td>
<td>&lt;2.8</td>
<td>0.81-4.02</td>
<td>1.9088</td>
<td>2.8030</td>
<td>3.1679</td>
</tr>
</tbody>
</table>

NA = not available.

* Normal solute/creatinine ratios may not be well established and universally accepted as adult normal reference values.

Based on these arguments, the Bland and Altman Test of Agreement is used to assess the agreement between the 24-hour urinary solute/creatinine ratios with the corresponding measurements from the early morning spot sample. If a simple visualization method compares the measurements by the 2 methods (Fig. 1), the “limit of agreement” is estimated by the mean difference in the paired values and their standard deviations. This limit is then used to judge on the agreement of the measurements by the 2 methods. If the value indicated by the “limit of agreement” is not clinically important, (which requires the variable points to lie on the line of equality), and if the value is reduced to half it would no longer agree with the variable measured in full strength value but the correlation coefficient would remain good. This means that if the measurement scale of a variable is reduced to half it would no longer agree with the variable measured in full strength value but the correlation coefficient would remain good. This means that if the measurement scale of a variable is reduced to half it would no longer agree with the variable measured in full strength value but the correlation coefficient would remain good. However, the correlation coefficient to the 24-hour urinary excretion as a good indicator for using the normal range of the defined measurement) then agreement is not clinically important, (which depends on the normal range of the defined measurement) then agreement can vary widely in range, thus ensuring a significant correlation.

1. Correlation coefficient (r) measures the strength of a linear relationship between the 2 related measurements. A correlation coefficient (r) will be high if the variables are related. A correlation coefficient (r) will be low if the variables are not related. A correlation coefficient (r) is not affected by the change in scale of measurement but agreement does. This means that if the measurement scale of a variable is reduced to half it would no longer agree with the variable measured in full strength value but the correlation coefficient would remain good.

2. Correlation coefficient (r) measures the strength of a linear relationship between the 2 related measurements. A correlation coefficient (r) will be high if the variables are related. A correlation coefficient (r) will be low if the variables are not related. A correlation coefficient (r) is not affected by the change in scale of measurement but agreement does. This means that if the measurement scale of a variable is reduced to half it would no longer agree with the variable measured in full strength value but the correlation coefficient would remain good.

3. A measurement with a larger range of true quantity in the sample will have a higher correlation, in which the variable points lie on the line of equality. The measurement scale of a variable is reduced to half it would no longer agree with the variable measured in full strength value but the correlation coefficient would remain good. However, the correlation coefficient to the 24-hour urinary excretion as a good indicator for using the normal range of the defined measurement) then agreement can vary widely in range, thus ensuring a significant correlation.
The data with DG(CaOx) value of 2.8 may lie somewhere before but close to 50th percentile, indicating that > 50% of the stone-formers have a supersaturated urine.

The 50th percentile is 2.8030, the 75th percentile is 3.1679, and the 100th percentile is 4.0200.

After adjustment for the possible overestimation of 1.274, the 50th, 75th and 100th percentiles of the data would be changed as follows. The percentages of data that are more than the limit of 2.8 will be as follows:

50th percentile: 2.8030 – 1.274 = 1.529
75th percentile: 3.1679 – 1.274 = 1.8939
100th percentile: 4.0200 – 1.274 = 2.746

Now, no data has a DG(CaOx) value of > 2.8. Thus, 50% or more stone-formers may be wrongly classified to have supersaturated urine if using the early morning spot urine instead of the 24-hour urine sample in estimating the urinary saturation.

Figure 2. Diagrammatic explanation on the measurement disagreement after adjustment for the possible overestimation by the early morning spot urine value compared to the 24-hour urine using the DG(CaOx) data of the stone-formers.

In conclusion, the early morning spot urine test cannot replace the 24-hour urine collection in the evaluation of urinary metabolic abnormalities in stone-formers. A good correlation does not translate to an agreement between the 2 measurements.

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References


