Dear Sir,

Since ammonium is the crucial component of renal acid excretion, the measurement of its urinary concentration represents a major diagnostic step in conditions affecting the urinary acid excretion [1-3]. The very cumbersome formaldehyde titration has been traditionally used for the measurement of urinary ammonium [4]. Colorimetric assays are technically simpler [5]. However, in most clinical laboratories, both formaldehyde titration as well as colorimetric assays are unsuitable for a bedside determination of urinary ammonium. An indirect estimate of urinary ammonium, the modified urine osmolal gap, has been more recently suggested [6]. The usefulness of the mentioned estimate was, therefore, evaluated in 34 healthy subjects (25 males and 9 females, age 5-44 years). The urinary ammonium concentration was assessed colorimetrically using a modification of the Berthelot reaction, replacing phenol by sodium salicylate [7]. In addition, the urinary ammonium concentration (mmol/l) was indirectly estimated using the modified urine osmolal gap [6]:

\[
\text{Osmolality} - \left[2(\text{sodium} + \text{potassium}) + \text{urea} + \text{glucose}\right] / 2
\]

Standard laboratory methods were used for the determination of osmolality (mmol/ kg) and sodium, potassium, glucose, and urea concentrations (mmol/l).

The agreement between measured and estimated urinary ammonium was assessed using the following table:

<table>
<thead>
<tr>
<th>P. Paolo</th>
<th>Meregalli</th>
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<tbody>
<tr>
<td>C. Christa</td>
<td>Lüthy</td>
</tr>
<tr>
<td>O.H. Oskar H.</td>
<td>Oetliker</td>
</tr>
<tr>
<td>M.G. Mario G.</td>
<td>Bianchetti</td>
</tr>
</tbody>
</table>

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Measured ammonium mmol/l
10  20  30  40
Average ammonium mmol/l

Fig. 1. Relationship between measured urinary ammonium and modified urine osmolal gap (estimated ammonium) in 34 subjects. The left panel depicts the linear correlation between measured and estimated ammonium concentrations ($y = 0.864x$, $r=0.621$, $p < 0.01$). The right panel depicts the difference against the mean value diagram suggested by Bland and Altman [7]. The urinary ammonium level estimated using the modified osmolal gap was on the average lower by 4.5 mmol/l than the measured one (–). The 95% limits of agreement are -43.2 and 34.4 mmol/l (○).

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using both a simple regression and the residual analysis recently suggested by Bland and Altman [8], usually reported as difference against the mean. Briefly, the difference between the two techniques was plotted against their mean, and the 95% limits of agreement were calculated from the mean difference and the corresponding standard deviation. The results are shown in figure 1. Like in the original paper [6], the relationship between measured ammonium and modified osmolal gap was found to be significant ($y = 0.864x$, $r=0.621$, $p < 0.01$). The urinary ammonium level estimated using the modified osmolal gap was on the average lower (by 4.5 mmol/l) than the measured one. On the other hand, the calculated 95% limits of agreement of -43.2 and 34.4 mmol/l indicate that 95% of the differences lie between the mentioned limits. Thus, the estimated urinary ammonium level may be 43.2 mmol/l below or 34.4 mmol/l above the measured level which seems unacceptable even for practical, bedside purposes.

The modified urine osmolal gap has been developed on the basis of (1) negligible excretions of cations such as calcium and magnesium and (2) an almost complete urinary dissociation of sulphate, phosphate, and organic salts. The results of our investigations and data from the literature disprove these assumptions [9].

In conclusion, our results indicate the unreliability of the modified urine osmolal gap for estimating the urinary ammonium concentration.

References
