Calculated vs Measured Plasma Osmolalities Revisited

C. I. Bhagat, P. Garcia-Webb, E. Fletcher, and J. P. Bellby

The osmolalities of 100 plasma samples were measured and compared with the osmolalities calculated from the plasma concentrations (mmol/L) of sodium, potassium, glucose, and urea by several different formulae. The formula recommended by Dorwart and Chalmers (Clin Chem 21: 190, 1975) gave inferior results to those obtained with our "most accurate" formula: osmolality = 1.89 Na + 1.38 K + 1.03 urea + 1.08 glucose + 7.45. We recommend using this formula for calculation of osmolality on equipment linked to a computer. However, for simplicity, and to reduce the possibility of calculation errors, the following formula can be used for manual calculations: osmolality = 1.86 (Na + K) + glucose + urea + 10.

Additional Keyphrases: electrolytes - osmolar gap

The osmolality of a solution depends on the total number of particles in the solution. In serum or plasma samples the difference between the measured and the calculated osmolality is the osmolar gap. This osmolar gap has been used to screen for drug overdose (1), especially alcohol (2), to estimate mannitol concentration in serum (3, 4), and to form prognoses of shock (5). Furthermore, although direct measurement of plasma osmolality is preferable, calculated osmolality might have to be used in smaller laboratories that do not have an osmometer.

Dorwart and Chalmers (6) compared 13 different formulae for calculating serum osmolalities and found that none were entirely satisfactory. Consequently they derived a formula themselves that gave the most nearly accurate calculated osmolality for their data:

\[
\text{osmolality} = 1.86 \text{Na} + \text{glu/18} + \text{blood urea nitrogen/28} + 9 \\
\text{(glucose and urea in mg/100 mL)}
\]

or

\[
\text{osmolality} = 1.86 \text{Na} + \text{glu} + \text{urea} + 9 \\
\text{(glucose and urea in mmol/L)}
\]

This formula has subsequently been incorporated into a commercial multichannel analyzer, the Astral 4 (Beckman Instruments Inc., Fullerton, CA 92621), so that the calculated osmolality is automatically printed out from the sodium, urea, and glucose results.

Our subjective impression on using the Dorwart–Chalmers formula was that the calculated osmolality was less than the measured osmolality, an impression we confirmed when we analyzed 100 samples. We report our findings and suggest two alternative formulae, which include a term for potassium.

Materials and Methods

We analyzed 100 plasma samples from hospitalized patients for sodium, potassium, and urea with a SMAC II (Technicon Instruments Corp., Tarrytown, NY 10591). The results for sodium and potassium, which were measured by ion-selective electrodes after predilution, were similar to those obtained by flame photometry. Urea was measured by the diacetylmoxime method. Glucose was determined with the Cobas Bio centrifugal analyzer (Roche Diagnostics, Dee Why, NSW 2103) by the hexokinase/glucose-6-phosphate dehydrogenase method. Osmolalities were measured in duplicate with an Advanced Digimatic Osmometer Model 3DB (Advanced Instruments Inc., Needham Heights, MA 02194) by freezing-point depression. The standard deviation for osmolality measurements from paired samples was 0.98 mmol/kg.

The patients in this study included 32 with renal failure, 13 with diabetes mellitus, four with hypernatremia (Na > 146 mmol/L), 30 with hyponatremia (Na < 134 mmol/L), and 42 others (including "normals"). Some patients were included in more than one category. The "most accurate" formula was derived by minimizing the sum of the squares of the difference of the estimated value from the average value, by using the Nelder–Mead simplex minimization procedure (7). To derive a simpler formula for manual calculation, we modified the Dorwart–Chalmers formula (Table 1, formula 3) to include a term for potassium, then

Table 1. Comparison of Measured Osmolalities with Calculated Osmolalities (n = 100)

<table>
<thead>
<tr>
<th>Formula</th>
<th>Difference, mmol/kg</th>
<th>( \bar{x} )</th>
<th>SD</th>
<th>SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. 1.86 (Na + K) + urea + glucose + 10</td>
<td>0.67</td>
<td>3.4</td>
<td>0.34</td>
<td></td>
</tr>
<tr>
<td>2. 1.86 (Na + K) + urea + glucose + 9</td>
<td>1.67</td>
<td>3.7</td>
<td>0.37</td>
<td></td>
</tr>
<tr>
<td>3. 1.86 Na + urea + glucose + 9 ( \pm )</td>
<td>9.08</td>
<td>9.8</td>
<td>0.98</td>
<td></td>
</tr>
</tbody>
</table>

*Measured osmolality minus calculated osmolality.

**Dorwart–Chalmers formula.

Department of Clinical Biochemistry, Queen Elizabeth II Medical Centre, Perth, Australia 6009.

Received May 18, 1984; accepted July 17, 1984.
minimized the difference between measured and calculated osmolality by adjusting the constant in the formula (Table 1, formula 1).

Results
Measured osmolalities were compared with osmolalities that were calculated according to the formulae listed in Table 1. Formula 1 gave the least mean difference between measured and calculated osmolalities and the best standard error of the mean (SEM) of the difference. Measured vs calculated osmolality by this formula is plotted in Figure 1 (left). The osmolalities of plasma ranged from 235 to 356 mmol/kg, and the results fell about the line of identity.

Figure 1 (middle) shows the results for the same samples calculated from formula 3, the Dorwart-Chalmers formula. All the calculated values fall below the line of identity and there is a greater scatter at higher osmolalities.

The formula we derived that gave the most nearly accurate calculated osmolality was:

\[ \text{osmolality} = 1.89 \text{ Na} + 1.38 \text{ K} + 1.03 \text{ urea} + 1.08 \text{ glucose} + 7.45 \]

This formula gave a mean difference between measured and calculated osmolalities of zero, a standard deviation (SD) of 3.2, and a SEM of 0.32. Figure 1 (right) shows that the results calculated with this formula fell about the line of identity, over the range of osmolalities studied.

The error between the calculated and measured osmolality will be less than 6.4 and 6.8 mmol/kg (2 SD), by our complex and simplified formulae, respectively.

Discussion
Several recent reports have suggested that the use of the Dorwart-Chalmers formula in calculating serum osmolality tends to underestimate the true osmolality of the sample (2, 8). Coakley et al. (2) found that in patients who had not ingested alcohol the measured osmolality in nearly all instances exceeded the calculated osmolality. Also Sklar and Linas (8) reported that the osmolal gap in controls was 8.8 ± 1.3 (SEM) milli-osmol/kg, with the measured osmolality exceeding the calculated osmolality. However, they erroneously stated that the osmolal gap was similar to that found by Dorwart and Chalmers, whereas the latter had derived the formula such that the osmolal gap was zero. In our results (Figure 1, middle) the measured osmolality in nearly all instances was greater than the osmolality calculated by the Dorwart-Chalmers formula. This discrepancy was not due to the use of plasma samples instead of serum. The osmolality of 10 paired samples of serum and plasma (in heparin anticoagulant) obtained at the same time showed no significant differences. The bias in our laboratory for the measurements of sodium, potassium, urea, glucose and osmolality, as assessed by external quality control, was negligible. We cannot offer any explanation for the marked discrepancy between our findings and those of Dorwart and Chalmers. Although there will be differences between the formulae derived from different studies, depending on the composition of the patient population studied, these differences will be minor.

The inclusion of the potassium value in calculating osmolality improved the SD of the difference from 9.8 (formula 3, Table 1) to 3.7 (formula 2). This is reflected in the changes in the scatter of data points about the line of identity in the sections of Figure 1. Because potassium is almost invariably measured at the same time the sodium, we think it should be included in the formula for calculating plasma osmolality. These formulae yielded similar results irrespective of whether the subjects were "normal," hypernatremic, or hyponatremic, or whether they had renal failure or diabetes mellitus. However, our derived formulae were not applicable in subjects who had hyperlipidemia or hyperproteinemia when we measured sodium and potassium by ion-selective electrodes, after predilution (ISEP); rather, they were applicable when sodium and potassium were measured by ion-selective electrodes directly without predilution (ISED). In a patient with triglyceride concentration of 17 mmol/L, the measured osmolality was 360 mmol/kg and the osmolality from calculated ISEP-determined values for sodium and potassium was 336 mol/kg; with ISED values, the calculated osmolality was 353 mmol/kg. In another patient, whose total protein concentration was 134 g/L, the measured osmolality was 285 mmol/kg, and the calculated osmolality was 265 mmol/kg (ISEP) and 285 mmol/kg (ISED).

We conclude that the continued use of the Dorwart-Chalmers formula can no longer be recommended and suggest that our most nearly accurate formula, calculated osmolality = 1.89 Na + 1.38 K + 1.03 urea + 1.08 glucose + 7.45, should be used in computer-linked equipment. For manual calculations we recommend the simpler formula, calculated osmolality = 1.89 (Na + K) + glucose + urea + 10, the mean difference and SD of the difference being similar to those obtained with the more complex formula.

References
The Quantab Strip in the Measurement of Urinary Chloride and Sodium Concentrations

Peter J. M. Sloan,¹ Gareth Beevers,¹ and Frances E. Baxter²

The "Quantab" strip (Ames) measures chloride in fluids. For sodium chloride solutions and urine we found very good correlations between the Quantab reading and the chloride concentration as measured by chemical assay \((r = 0.95\) for chloride and \(r = 0.85\) for sodium in urine). The strip gave reproducible results over the temperature range 4 to 37 °C. There was very little inter- and intra-observer variation in reading the strip. Although 10 to 23 min is required to complete the reaction, the strip reading is stable thereafter. We suggest that the strip could be useful in epidemiological studies of urinary sodium concentration and clinically in helping patients adhere to a low-salt diet.

Additional Keyphrases: screening · dipsticks · self-testing · electrolytes

The "Quantab" chloride titrator strip (Ames Division, Miles Laboratories Ltd., Slough, Berks., U.K.) is a 78 × 13 mm plastic strip with an attached capillary column impregnated with silver dichromate, which is brown. When a strip is placed in the solution under test, fluid passes up the column from the bottom by capillary action and chloride ions react with the silver ions to form white silver chloride. When the solution reaches the top of the capillary column, an orange moisture-sensitive band turns black, whereupon a reading can be taken from the strip. The chloride concentration of the solution determines the level of the meniscus between white and brown. The reading is taken from the highest point on the meniscus across to divisions drawn on the sides of the strip. The scale is from 0 to 10, in arbitrary units with 0.2-unit division lines (Figure 1).

The strip has been used for many years for measuring the chloride concentration of water for swimming pools and concrete manufacture, but recently it has been used clinically. In four studies (1-4) the strip was used in an assessment of sodium chloride excretion, with good correlation between strip reading and urinary chloride concentration. In this, the first formal assessment, we have compared the strip reading with previously determined chloride and sodium concentrations in urine and standard sodium chloride solutions. Stability, reproducibility, and speed of reaction were estimated, as was intra- and interobserver variability in reading the strip.

Materials and Methods

Urine correlations. The strip was used to estimate the chloride concentration of 128 urine samples obtained from volunteers while they were taking high-, normal-, and low-salt diets. The strips were read by one observer (P.J.M.S.) and the urinary chloride concentration was evaluated by coulometry, with the Corning 920 chloride meter. Sodium was measured with a Model 545 flame photometer (Instrumentation Laboratory, Lexington, MA 02173).

Chloride solution correlation. The strip was used to estimate the chloride concentration of sodium chloride solutions of known strengths (0, 10, 25, 50, 100, 150, 200, 300, and 400 mmol/L).

Reaction time. The time taken for the orange moisture-sensitive band on the "Quantab" strip to turn black was measured in 58 instances. The strip was then viewed after

---

¹ University Department of Medicine and ² Department of Clinical Chemistry, Dudley Road Hospital, Birmingham B18 7QH, U.K. Received May 25, 1984; accepted July 12, 1984.