Evaluation of the “Auto-Stat 6010” Automatic Osmometer and Its Comparison with the “Digimatic-Advanced 3DII” Manual Osmometer

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Summary: The results are presented of a comparative study between two osmometers, a manual one, Digimatic-Advanced 3DII (Advanced Instruments, Medical Europa, Barcelona), and an automatic one, Auto-Stat 6010 (Kyoto, Daiichi, Kagaku, Menarini, Firenze). Both osmometers have the same operation principle, but they employ different systems for determination of the freezing point depression. Both instruments showed good precision (CV < 1%), accuracy, and a wide range of linearity. In the assay of 133 sera and 101 24-h urines, the methods showed a good correlation (r = 0.945 and r = 0.999) and the Anova test showed no statistical difference between the means (p > 0.05). The carry over effect in the Auto-Stat was statistically significant (p < 0.001) but within the range of imprecision of the osmometers. Variation due to evaporation is lower than 0.8%. In conclusion, we are sure that both osmometers are useful in the laboratory, although the Auto-Stat 6010 osmometer has the advantage over the Digimatic-Advanced 3DII of automatic sample processing.

Introduction

Osmolality is a colligative property of solutions which depends only on the number of dissolved particles present in the solution, and not on their size or charge (1). High values of serum osmolality can be found in diabetes, kidney insufficiency, or after poisoning by certain compounds, e.g. salicylates, barbiturates, alcohol (2–4). In the evaluation of kidney function the ratio between urine osmolality and serum osmolality can be very useful; this ratio decreases to 1 in chronic kidney insufficiency and is below 1 in inasipid diabetes (5, 6). Osmolality is therefore a very important quantity in the study of pseudohyponatraemia (7) and rehydration (8). Urine and plasma osmolality are more useful in the diagnosis of hydration than are changes in haematocrit, serum proteins, or urea, which are more dependent on factors other than hydration (9).

In the clinical laboratory, a quick and reliable method is necessary for the determination of osmolality in biological fluids, in both emergency and routine situations. Most osmometers used in clinical laboratories measure the freezing point depression of the sample (1).

The aim of this paper is to compare two osmometers, a manual one, Digimatic-Advanced 3DII (Advanced Instrument, Medical Europa), and an automatic one, Auto-Stat 6010 (Kyoto, Daiichi, Menarini). Both have the same operation principle, but they employ different systems for determination of the freezing point depression. Some of the automated features of the Auto-Stat 6010 osmometer are also appraised.

Materials and Methods

Instruments

Automatic osmometer

Auto-Stat 6010 (Kyoto, Daiichi, Kagaku, Menarini, Firenze (Italy))

This osmometer employs the freezing point depression method. The cooling system is thermally controlled by thermo-modules, while a thermistor sensor monitors the temperature of the sample. After suction of sample into the measuring cell, the sample in the thermal measuring block is gradually cooled, and as the liquid temperature is lowered to below freezing point, the sample remains liquified without crystallizing (supercooled). At this point, an electric current is applied to the thermo-module, then the sample in the cooling block is further cooled, and spontaneously frozen. Simultaneously the sample in the thermal measuring block is also instantly crystallized, and becomes as mixture of ice and solution. The temperature of this mixture is the freezing point of the solution and is inversely related to osmolality.

This osmometer is fully automatic. Samples are taken by a mobile arm from a 33-sample disk with 3 calibrators.

Manual osmometer

Digimatic-Advanced 3DII (Advanced Instrument, Medical Europa, Barcelona (Spain))

This osmometer also employs the freezing point depression method, but with a different freezing system. The sample is cooled by a bath of propylene glycol antifreeze solution at
-5 °C until its temperature falls below the equilibrium freezing point. Crystallization is then induced by vigorous stirring. The heat released by the formation of the ice crystals raises the temperature of the sample until the rapid freezing stops and an equilibrium temperature is established. The temperature at this equilibrium is the freezing point of the solution, and is inversely related to osmolality.

Methods

Intra- and inter-assay precision was investigated at 3 osmolalities using commercial controls (2 sera and 1 urine sample, Ciba Corning Diagnostics Corp., Irvine, CA, USA). For inter-assay precision, one assay per day per concentration was performed for 20 days. For intra-assay precision, 20 assays per concentration were performed on the same day.

Commercial aqueous standard solutions of 100, 500, 900 mosmol/l (Advanced Instruments, Inc.) and 290 mosmol/l (Clinitrol 290, Advanced Instruments, Inc.) were used for the accuracy test (10).

Analytical recovery was determined by twice assaying an aqueous 900 mosmol/l standard (Advanced Instruments, Inc.), or different dilutions of this standard with serum. The serum osmolality was the average obtained from assaying the serum sample 30 times in each osmometer. The averages were 292.7 mosmol/l (Digimatic-Advanced 3DII) and 294.2 mosmol/l (Auto-Stat 6010). For an osmolality of 90 mosmol/l the volume ratio serum: standard was 9:1, and for osmolalities of 180 and 270 mosmol/l the ratios were 8:2 and 7:3, respectively. To calculate the recovery (measured result/theoretical result) we always took into account the effect of serum dilution by adding an aqueous standard.

To appraise the recovery, the upper and lower confidence limits of the mean recovery were calculated by the expression “Mean recovery ± 2.776 SD” (2.776 = t-test statistics, n = 5, p < 0.05) for each quantity added. The recovery is considered to deviate significantly from the theoretical, if the theoretical recovery does not lie inside these limits.

Linearity was tested by means of a standard solution of 900 mosmol/l and aqueous solutions of 50, 100, 200, 400, and 600 mosmol/l made from this standard. Every solution was assayed 10 times in each osmometer (11).

To compare both osmometers, 133 sera and 101 urines (24-hour samples) from patients of the Nephrology Department were assayed. All the samples were obtained by standard methods and processed on the same day.

Means were compared, using the Anova-one way test (statistics software Epistat) (12). Also, the correlation coefficients of Pearson, and the regression equations according to Passing & Bablok were calculated (13-15).

Results

Precision

Table 1 shows the results for the inter- and intra-assay precision of both osmometers.

<table>
<thead>
<tr>
<th>Level</th>
<th>Inter-assay</th>
<th>Intra-assay</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I</td>
<td>II</td>
</tr>
<tr>
<td><strong>Digimatic-Advanced 3DII</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Mean (mosmol/l)</td>
<td>461.00</td>
<td>522.55</td>
</tr>
<tr>
<td>SD</td>
<td>4.22</td>
<td>3.61</td>
</tr>
<tr>
<td>CV (%)</td>
<td>0.92</td>
<td>0.69</td>
</tr>
<tr>
<td><strong>Auto-Stat 6010</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Mean (mosmol/l)</td>
<td>472.45</td>
<td>532.55</td>
</tr>
<tr>
<td>SD</td>
<td>3.97</td>
<td>5.06</td>
</tr>
<tr>
<td>CV (%)</td>
<td>0.84</td>
<td>0.95</td>
</tr>
</tbody>
</table>
Accuracy

Figure 1 and table 2 show the results of the reference standards obtained with both osmometers.

Figure 2 shows the analytical recovery. In both osmometers the recovery was not statistically different from the theoretical value.

Table 2. Accuracy at four concentrations of osmolality. Measured value is the mean of 10 determinations. Percentage of deviation is calculated as \((100 - (\text{measured value} \times 100)/\text{theoretical value}))\).

<table>
<thead>
<tr>
<th>Theoretical value (mosmol/l)</th>
<th>Measured value (mosmol/l)</th>
<th>Deviation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Digimatic-Advanced 3DII</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100</td>
<td>99</td>
<td>1</td>
</tr>
<tr>
<td>290</td>
<td>285</td>
<td>1.7</td>
</tr>
<tr>
<td>500</td>
<td>500</td>
<td>0</td>
</tr>
<tr>
<td>900</td>
<td>911</td>
<td>1.2</td>
</tr>
<tr>
<td><strong>Auto-Stat 6010</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100</td>
<td>101</td>
<td>1</td>
</tr>
<tr>
<td>290</td>
<td>292</td>
<td>0.7</td>
</tr>
<tr>
<td>500</td>
<td>507</td>
<td>1.4</td>
</tr>
<tr>
<td>900</td>
<td>904</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Linearity test

Figure 3 shows the linearity results obtained from several dilutions of a standard solution of 900 mosmol/l on both osmometers.

Comparison methods

Table 3 shows the comparison of the mean osmolalities for sera and urine determined on the two osmometers, using the Anova one way test.

Figures 4 and 5 show the correlation coefficients and regression equations for the patient sera and urine samples.

Effect of carry over

The effects of carry-over are shown on table 4.

Effect of evaporation

The variations produced by evaporation in the Auto-Stat 6010 are shown on table 5.

![Graph](https://example.com/graph.png)
Fig. 4. Comparison of methods. Measured osmolality of 101 urines (24 hour collections) by both osmometers.
\[ y = -4.905 + 1.004 \times, r = 0.999 \]

Fig. 5. Comparison of methods. Measured osmolality of 133 sera by both osmometers.
\[ y = 23.708 + 0.917 \times, r = 0.945 \]

Tab. 4. Effect of carry over in a 100 mosmol/l sample by the Auto-Stat 6010. Means are significantly different by test ANOVA (p < 0.001).

<table>
<thead>
<tr>
<th>Sample after a solution of 900 mosmol/l</th>
<th>n</th>
<th>( \bar{x} ) (mosmol/l)</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample</td>
<td>15</td>
<td>100.53</td>
<td>0.52</td>
</tr>
<tr>
<td>Sample after a solution of 900 mosmol/l</td>
<td>15</td>
<td>101.86</td>
<td>0.51</td>
</tr>
</tbody>
</table>

Assay throughput

The time spent in calibrating the Auto-Stat 6010 osmometer is 8 minutes and 40 seconds, and it takes 1 hour and 20 minutes to process the 33 samples. The mean speed is 26 samples/hour for the Auto-Stat 6010 and 30 samples/hour for the Digimatic-Advanced 3DII osmometer.

Discussion

Clinical laboratory osmometers are required to provide quick and reliable results.

In the present study, both of the assessed osmometers showed good precision. In all cases the coefficients of variation are about 1%, and lower than 1.1-1.8%, which are the limits of the coefficients of interlaboratory variation for osmolality in the normal reference interval, according to the quality control of the North American College of Pathologists (18). Both osmometers show a better precision than 1.4-2.8%, which is the precision range of other commercial osmometers (19). The difference between the means of the two osmometers is possibly due to the effect of the serum matrix. The composition of the matrix (serum; specific serum proteins, such as albumin; polyvinylpyrrolidone) may differ from native serum in viscosity, physical interaction of low-molecular-mass substances with proteins, and with respect to Donnan and other charge-related phenomena. Thus, it is logical to expect differences between the behaviour of quality control specimens and that of fresh specimens from patients (20).

With respect to accuracy, our measured osmolality for the reference standards is very near to the theoretical osmolality. In all cases the percentage deviation is lower than 2%. Both osmometers present very similar results (tab. 2).

The recovery results are very similar for both osmometers. Recoveries were 1.002-1.033 for the Auto-Stat 6010, and...
0.992—1.024 for the Digimatic-Advanced 3DII. In both osmometers the recovery was not statistically different from the theoretical recovery (p > 0.05).

Both instruments gave a linear response over a wide range. The deviation of measured osmolality from the theoretical value was less than 1% for each dilution; except at the lower concentration of 50 mmol/l, where both instruments showed a deviation of 1—2%.

Comparison of the mean measured osmolalities of sera and urine, using the Anova-test, showed no statistically significant differences between the two osmometers (p > 0.05). The coefficient of correlation was good and the regression line slope was close to 1.

Variation due to evaporation in the Auto-Stat 6010 is lower than 0.8%, and there is no significant difference (p > 0.05) between the means.

Although the carry-over effect in the Auto-Stat 6010 is statistically significant, the resulting increase is within the range of the imprecision of the osmometers.

In conclusion, the Auto-Stat 6010 osmometer has the advantage over the Digimatic-Advanced 3DII of automatic processing of samples. This obviates the need for the presence of a technician during the analytical run, which compensates for the slower operation of the Auto-Stat 6010. The Digimatic-Advanced 3DII osmometer is particularly useful in the emergency laboratory, where the speed and simplicity of the test is very important.

References


