Sodium Measurements in Multiple Myeloma: Two Techniques Compared

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Sodium was determined by flame photometry and by direct potentiometry in 56 serum or plasma samples from 24 patients with multiple myeloma or macroglobulinemia. We observed differences between the two techniques as large as 17 mmol/L (12%). The flame-photometric values decreased relative to the direct-potentiometric values as protein increased or water content decreased. Moreover, the two sodium measurements could not be interconverted simply on the basis of correcting for protein or water content. There was significantly lower residual variance (p < 0.005) when the direct-potentiometric sodium values were compared with the osmolality (corrected for the influence of glucose and urea nitrogen) than when the flame-photometric values for sodium were compared. We conclude that direct potentiometric measurements of sodium in patients with multiple myeloma gives clinically relevant results but flame photometry does not. Clearly, the method by which sodium is measured in patients with multiple myeloma must be considered if results are to be interpreted correctly.

Additional Keyphrases: flame photometry · potentiometry · electrolytes · anion gap

Measurement of sodium in plasma by flame photometry may give artifactual low values in samples that have above-normal lipid (1-8) or protein (9-12) concentrations. The reason for the low values in hyperlipemia is the decreased percentage of water (water content) in plasma (1, 3, 8), which leads to there being less sodium in a given volume of the sample taken for analysis, even though the concentration of sodium in the water phase may be unaltered. For patients with multiple myeloma, the low sodium values have been explained by a similar influence of hyperproteinemamia on water content (9, 10, 19), the cationic nature of some of the paraproteins (10, 11), or an error in sampling owing to the high serum viscosity (12).

Studies in this laboratory (14, 15) and others (16, 17) have shown that values for sodium obtained by direct potentiometry (electrode measurement of sodium without sample dilution) are unaffected by increasing concentrations of albumin or other normal human proteins. In contrast, progressively decreasing values are found by flame photometry or indirect potentiometry (electrode measurement of sodium with sample dilution) under identical experimental conditions (14). Moreover, direct potentiometry of sodium gave a substantially higher value than flame photometry in one patient with multiple myeloma (18). All three of these analytical techniques are now commonly used by clinical laboratories.

To clarify the measurement of sodium in patients with multiple myeloma, we determined sodium by direct potentiometry and flame photometry of 56 samples from 24 such patients. Our data show that values by direct potentiometry agree best with osmolality measurements and that information on protein concentration or water content cannot be used to correct the low flame-photometric values.

Materials and Methods

Patient Group

The patients studied were initially identified on the basis of a total serum protein concentration >90 g/L on admission to Barnes Hospital or (in a few cases) by a history of multiple myeloma. Electrophoresis on cellulose acetate was then performed on all samples. Patients whose serum did not exhibit a paraprotein were included in a control group. Samples that showed a paraprotein were examined further by immunoelectrophoresis to establish heavy- and light-chain type. Samples (serum or heparinized plasma) from patients having a paraprotein were collected periodically over a 12-month period whenever the patient was admitted to the hospital or clinic. The diagnosis of multiple myeloma or Waldenstrom's macroglobulinemia was established by clinical, radiological, and bone-marrow biopsy criteria (19). The patient group included 19 patients with IgG, 14 with kappa light chains and five with lambda light chains; three patients with IgA, one with kappa and two with lambda light chains; and two patients with IgM and kappa light chains.

Control Group

The control group consisted of samples from individual patients with a wide range of protein values. None exhibited a paraprotein on cellulose acetate electrophoresis but four of the subjects had a polyclonal increase in the γ-globulin region.

Methods

Sodium was measured by direct potentiometry, with a Nova-1 sodium/potassium analyzer (Nova Biomedical Inc., Newton, MA 02164), and by flame photometry, with a Beckman KLiNA flame (Beckman Instruments Inc., Fullerton, CA 92834). This flame photometer has been previously shown not to produce errors ascribable to changes in sample viscosity (14). The two instruments were standardized with the same standard solution containing, per liter, 140 mmol of NaCl and 4 mmol of KCl. All sodium values were measured in duplicate or triplicate and averaged. Total protein was measured by the biuret reaction, albumin by the bromcresol green reaction, glucose by reaction with hexokinase, and urea nitrogen by reaction with urease—all with the Automated Clinical Analyzer (aca; Du Pont Co., Clinical Systems Division, Wilmington, DE 19898). Osmolality was measured by freezing-point depression (Advanced Digimatic Osmometer, Model 3D; Advanced Instruments Inc., Needham Heights, MA 02194).

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The osmolality was corrected for the influence of glucose and urea nitrogen by use of the formula (20):

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\text{Corrected osmolality} = \text{measured osmolality} - \left( \frac{\text{glucose} + \text{urea nitrogen}}{18 + 2.8 + 9} \right)
\]

The direct-potentiometric and flame-photometric sodium values were compared with the values for corrected osmolality. The significance of the differences in the residual variances about the fitted regression lines was assessed by the F-test.

Water content was measured by placing 100 μL of serum (SMI micro/pettor series I; SMI, Berkeley, CA 94710) into a preweighed weighing vial. After reweighing, the sample was heated at 110 °C overnight, cooled in a desiccator, and reweighed. A density of water of 1 g/mL was assumed and the water content was calculated as the loss in weight, in milligrams per 100 μL, and expressed as a percentage.

Results

Sodium values averaged 144.4 (SD 5.0) mmol/L by direct potentiometry and 138.8 (SD 6.4) mmol/L by flame photometry for the 56 samples from 24 patients with plasma cell myeloma or Waldenstrom's macroglobulinemia. For the 41 patients in the control group, the respective sodium values were 141.9 (SD 5.5) mmol/L and 140.6 (SD 5.0) mmol/L. Thus there was a significantly larger (p < 0.001) discrepancy between the two techniques of measuring sodium in the patient group [5.6 (SD 4.1) mmol/L, range 3.3 to 17.3] than in the control group [1.3 (SD 3.6) mmol/L, range 4.8 to 9.2].

Figure 1 shows the influence of protein values on the relationship between the two methods of measuring sodium in the patient group. Clearly, the ratio of flame-potentiometric values to direct-potentiometric values decreases as protein increases. The correlation coefficients and scatter of the data make it apparent that information as to total protein content is not sufficient to enable the results by one method of measuring sodium to be accurately predicted from results by the other. Similar data were obtained when we used results for globulin (total protein − albumin) instead of total protein (data not shown).

Because one of the major influences of the protein concentration would be to alter the water content of the plasma we compared the ratio of flame-photometric to direct-potentiometric values with the measured water content (Figure 2). The correlation coefficient and scatter of the data point were not improved by considering water content rather than total protein. In fact, the two methods of measuring sodium showed relative differences as great as 12%, which could not be totally accounted for by knowledge of total protein or water content.

We compared values for sodium by direct potentiometry (Figure 3A) and by flame photometry (Figure 3B) with corrected osmolality values. The residual variances (S\(_{r}^2\)) about the fitted regression line were significantly less for the direct-potentiometric values (7.3) than for the flame-photometric values (18.4). This indicates that values by direct potentiometry agree more closely with osmolality measurements.

Discussion

Our data confirm that sodium values may be artifactual low in patients with multiple myeloma when measured by flame photometry (9–12)—or, presumably, by indirect potentiometry. We assume that flame-potentiometric value could also be low in patients with benign monoclonal gammopathy, but have not tested such patients. In contrast, sodium measurements by direct potentiometry give values in agreement with those predicted by osmolality measurements. This is in keeping with the expectation that direct potentiometry measures the activity of sodium in the water phase rather than the total sodium concentration; therefore it should not be affected by changes in water content resulting from varying protein content (14).

We were surprised that information concerning protein concentration or water content did not allow us to predict on sodium value from the other, and we cannot explain this. An analytical problem with one of our techniques is possible but doubtful, because the interassay precision (CV) of the sodium techniques is <1.5%. In addition three of the samples showing...
We conclude that direct-potentiometric measurement of sodium is more clinically relevant than flame-photometric measurement. Plasma osmolality or direct-potentiometric sodium values should therefore be used to assess sodium homeostasis of patients with multiple myeloma. Furthermore, knowledge of protein, globulin, or water content values cannot be used to interconvert the values obtained by the different measurement techniques. Because a given laboratory may be able to analyze sodium by all of these techniques, the clinician must be made aware of the method used to measure sodium in patients with multiple myeloma if he is to interpret the values correctly.

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References

17. Shyr, C., and Young, C. C., Effect of sample protein concentration


