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Brief Communications

A Simple Equation to Estimate the Osmolarity of Neonatal Parenteral Nutrition Solutions

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ABSTRACT. A predictive equation of osmolarity that correlates closely with the measured osmolality was determined. Taking into account that an osmometer is not available in most clinical settings, the proposed equation appears to provide a quick and simple osmolarity calculation of neonatal parenteral nutrition solutions. *Objective:* We measured the osmolalities of neonatal parenteral nutrition (PN) solutions to determine if these values may be predicted by a simple equation for calculation of their osmolarity values. *Methods:* The osmolalities of 101 consecutive different final PN admixtures, prepared for 36 neonates, were measured by the freezing point depression method. The respective intra-assay and interassay coefficients of variation were always <2.1%. Linear multivariate regression analysis was used to determine a predictive equation of osmolarity that correlates closely with the value of measured osmolality. *Results:* The mean (SD) osmolality of the final PN admixtures was 749.7 (165.4) mOsm/kg. The best-fitted equation, with a coefficient of discrimination R^2 = .95 (R^2 = .90 for samples between 500 and 1000 mOsm/L) is osmolarity (mOsm/L) = (nitrogen × 0.8) + (glucose × 1.235) + (sodium × 2.25) + (phosphorus × 5.43) - 50, with the concentration of components in mmol/L. Adapting the equation in our daily practice, using g/L for glucose and amino acids, mg/L for phosphorus, and mEq/L for sodium, the equation is osmolarity (mOsm/L) = (amino acid × 8) + (glucose × 7) + (sodium × 2) + (phosphorus × 0.2) - 50, with a similar R^2. *Conclusions:* Taking into account that an osmometer is not available in most clinical settings, the proposed equation appears to provide a quick and simple osmolarity calculation of neonatal PN solutions, thus allowing more accurate decisions to be taken regarding the choice of route and rate of administration of PN solutions. (*Journal of Parenteral and Enteral Nutrition* **28:**34–37, 2004)

The composition of parenteral nutrition (PN) solutions varies according to the age and condition of the patients. In order to promote growth and deliver an appropriate nutritional supply, high concentration of nutrients, minerals, and vitamins are usually administrated parenterally to neonates, thereby resulting in hyperosmolar PN solutions. This problem is even more acute in the case of preterm infants.[1,2] It is important for those caring for neonates to have quick and easy access to the osmolality values of infused PN solutions. This knowledge will allow more accurate decisions when choosing the route for administration and thereby make it easier to monitor potential risks related to infusion of hypertonic solutions peripherally.[3–5] Routine measurement of osmolalities of substances is not feasible in intensive care units. Some equations and methods have been proposed for the calculation of osmolarities of PN solutions according to their components.[6,7] Nevertheless, most of these equations were not derived from PN solutions prepared especially for neonates.

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The aim of this study is to determine if measured osmolalities of PN solutions prepared for newborn infants may be predicted by the osmolarity values of the same solutions estimated by a simple equation.

MATERIALS AND METHODS

The osmolalities of 101 consecutive different final PN admixtures prepared for 36 neonates were measured. The mean (SD) gestational age of these patients was 32.8 (4) weeks, the mean (SD) birth weight was 1931 (978) g, and prematurity and surgical conditions were the most common diagnoses.

The PN solutions were prepared in the Department of Pharmacy at Hospital Dona Estefânia. Special attention was paid toward the most precise calculation mode and the measurement of volumes of commercial solutions needed for the preparation of PN mixtures used in this study.

The solutions and commercial formulations used included the following: dextrose 30% or 50% (Labesfal, Tondela, Portugal), composed amino acids 6.5% with taurine (Vaminolact; Fresenius Kabi, Graz, Austria), calcium gluconate 10% (Labesfal), calcium chloride 10% (Labesfal), potassium chloride 7.5% (Labesfal), sodium chloride 20% (Labesfal), sodium acetate 13.6% (Labesfal), potassium acetate 9.8% or 19.6% (Labesfal), sodium glycerophosphate (Glycophos; Fresenius Kabi, Halden, Norway), magnesium sulfate 20% (Labesfal),

water-soluble vitamins (Soluvit N; Fresenius Kabi, Puurs, Belgium), trace elements (Peditrace; Fresenius Kabi), and heparin sodium 5000 IU/mL (Heparin Leo Pharmaceutical, Denmark).

In order to achieve the best homogeneous solutions in the final samples, PN admixtures were taken after a gentle shaking of each PN solution bag. A single investigator (L. P-S.) analyzed all the samples blindly. Using the previously reported methodology,[8] osmolality by freezing point depression was measured using an Osmomat 030 automatic cryoscopic osmometer (Gonotec, Inc, Germany). The osmometer used is programmed to sample volumes of 50 μL and reproducibility $< \pm 2\%$. Calibration of the osmometer using standard solutions was performed after every 30 measurements. Samples from the same PN bag were collected on 3 different occasions and analyzed to determine the interassay coefficient of variation. Each single sample was measured in triplicate in order to determinate the intra-assay coefficient of variation. Both the intra-assay and interassay coefficients of variation were always <2.1%.

Pearson or Spearman correlation tests were used for bivariate analysis between each component of the final PN admixture and measured osmolality (as adequate for parametric or nonparametric analysis). Linear multivariate regression analysis was used to determine a predictive equation of osmolarity that correlates closely with the value of osmolality. All the components of the final PN admixtures were initially considered for the determination of the equation. To achieve an equation that would be simultaneously accurate and simple, both "step by step" and "enter" methods were applied to exclude components that were superfluous for the equation, ie, components whose presence or absence in the equation did not modify the coefficient of discrimination and their association with osmolality had a multivariate significance of <0.05. A coefficient of discrimination (R^2) 0.9 or higher was considered as reflecting a good clinical correlation between measured osmolality and calculated osmolarity.

All statistical analysis was performed with Microsoft Excel 2000 and SPSS 6.1.3 (SPSS Inc, Chicago, Ill) statistical packages.

RESULTS

The mean (SD) osmolality of the final PN admixtures was 749.7 (165.4) mOsm/kg, ranging from 405.3 to 1166.0. Only 10% of the PN admixtures had osmolality <500 mOsm/kg, and 20% of the PN admixtures had osmolality >875 mOsm/kg.

The studied PN admixtures provided the patients the following daily supply per kilogram body weight (mean ± SD): amino acids (A) 1.7 ± 0.7 g, glucose (G) 11.6 ± 3.2 g, sodium (Na) 3.2 ± 1.2 mEq, chloride (Cl) 2.95 ± 0.8 mEq, potassium (K) 1.9 ± 0.6 mEq, calcium (Ca) 42.5 ± 8 mg, phosphorus (P) 24.8 ± 5.2 mg, and magnesium (Mg) 3.4 ± 4.25 mEq. These components achieved the following mean (SD) concentrations (mmol/L) in the final PN admixtures: N 158.6 (73.6), G 482.7 (112.0), Na 23.4 (7.7), Cl 22.4 (7.1), K 14.4 (4.6), Ca 8.3 (2.4), P 6.3 (1.9), and Mg 1.7 (2.1).

Among the various components of the final PN admixture, the concentration of glucose correlates better with the osmolality of the final admixture ($R^2 = .72$) than the concentration of any other single component. A final glucose concentration of ≥70 g/L has a positive predictive value of 97% for an osmolality of ≥600 mOsm/L (although with a negative predictive value of 75%).

Analyzing the measured osmolality for different final amino acid and glucose concentrations, it is possible to provide a general rule of thumb for the approximate osmolality of the final PN admixtures for extreme concentrations of both nutrients, as shown in Table I. Lower glucose concentration (<60 g/L) did not associate with high amino acid concentration or with osmolality ≥600 mOsm/L. On the other hand, high glucose concentration (>80 g/L) did very frequently associate with high osmolality, independently of the amino acid concentration. For intermediate glucose concentration (60 to 80 g/L), high osmolality was most frequently associated with amino acid concentration of ≥10 g/L.

Using either "step by step" or "enter" methods of linear multivariate regression analysis, on all the components of the final PN admixtures, similar results were obtained. The components that influence osmolality of the PN solutions the most were N, G, Na and P, the other components were always considered superfluous for the equation.

Using the concentration of each component in mmol/L (Fig. 1), the best-fitted equation with a coefficient of discrimination $R^2 = .95$ ($R^2 = .90$ for samples between 500 and 1000 mOsm/L) is:

$$\text{Osmolarity (mOsm/L)} = (N \times 0.8) + (G \times 1.235) + (\text{Na} \times 2.25) + (P \times 5.43) - 50.$$

Adapting for our daily practice of using g/L for G and A, mg/L for P, and mEq/L for electrolytes (Fig. 2), a similar R^2 is reached by the equation:

$$\text{Osmolarity (mOsm/L)} = (A \times 8) + (G \times 7) + (\text{Na} \times 2) + (P \times 0.2) - 50.$$

This equation was derived taking into account that the used amino acid solution (Vaminolact; Fresenius Kabi) contains 7 g of A per g of N.

TABLE I
Measured osmolality according to different amino acid and glucose concentrations in the final PN admixture (with usual mineral and electrolyte concentrations)

Osmolality mOsm/kg (cases)	Glucose concentration		
	Glucose <60 g/L	Glucose 60–80 g/L	Glucose 80–120 g/L
Amino acid concentration			
<10 g/L	<500 (8)	500–625 (7)	550–907 (8)
10–20 g/L	520 (1)	540–730 (16)	553–941 (39)
>20 g/L	—	744–1050 (4)	745–1166 (18)

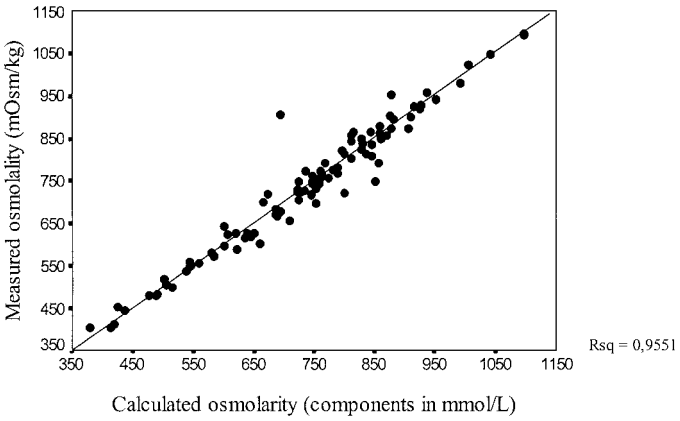

FIG. 1. Prediction of the osmolality of PN solutions by calculated osmolarity, from components in mmol/L: osmolarity (mOsm/L) = (N × 0.8) + (G × 1.235) + (Na × 2.25) + (P × 5.43) - 50.

DISCUSSION

The osmolality of a given solution depends on the number of molecules of solute in the solvent and is expressed in milliosmoles of solute per kilogram of solvent. It is not convenient, and it may be inaccurate, to calculate the osmolality of a multicomponent solution simply by summing up the osmolality values of starting solutions.[9] Osmometry is the reliable method to measure the osmolality of a solution.[10] Compared with vapor-pressure osmometry, the freezing point depression method is preferable when solvent volatile substances are measured.[10,11]

Osmolarity differs from osmolality because it is a measure of milliosmoles of solute per liter of solution. Osmolarity has gained acceptance in the clinical setting because of the convenience of expressing concentration on a volume basis.[6] Both terms have been used interchangeably, and their values do not differ significantly for diluted nonelectrolyte solutions. In our study, the magnitude of the values for both measured osmolality and calculated osmolarity of the final PN admixtures are in fact very similar. However, in some concentrated solutions containing electrolytes, the osmolality values may eventually differ significantly from the osmolarity values.[6]

Several authors have reported an increased risk of peripheral phlebitis and infiltration using peripheral route for infusion of PN solutions around ≥600 mOsm/L.[3,12,13] Although hyperosmolality of infused solutions is recognized as a major factor for the endothelial damage, other factors may contribute to peripheral phlebitis.[4] It is demonstrated that reducing the infusion rate of hypertonic PN solutions still increases the duration of infusion and risk of phlebitis.[3,14] Thus, health care providers in special care nurseries should have easy access to the osmolality of PN solutions that are being infused, particularly when they are suspected to be hypertonic. As the equipment for osmometry is relatively expensive and not available in most clinical settings, different equations have been proposed for the estimation of osmolarities of PN solutions according to some of their components.[6,7] These PN solutions are generally manufactured in hospitals according to patients' needs according to simpler solutions that are commercially available. Accordingly, the components influencing the osmolality of PN solutions vary, depending on the age and specific needs of the patient. Some equations for calculation of osmolarity of pediatric PN solutions[7] are based on the G and A values and do not include some components provided in proportionally larger amounts to preterm neonates, such as phosphorus or calcium.[1,2,15,16] Hence, the equations for estimation of osmolarity of neonatal PN solutions should be validated and derived from admixtures especially prepared for newborn infants. A simple and easy-to-use equation should include as few components as necessary to provide a reliable estimate of osmolarity of the solution.

Linear multivariate regression analysis performed with all the components of the final PN admixtures proved that N, G, Na, and P have the major influence on the calculation of osmolarity for correlation with osmolality of the analyzed neonatal final PN solutions, allowing for the calculation of a quite simple equation. The osmolarity estimated by the proposed equation allows an excellent practical prediction of the measured osmolality, considering the concentration of the components in mmol/L. Another equation, also with a good coefficient of discrimination, was obtained using the concentration of the components as mass per liter or as mEq per liter, units more frequently used in clinical practice. The accuracy of the proposed equation as a predictive tool for the osmolality of the final PN admixtures is much better than using the concentration of any of the components alone, or even 2 of them together, as using the general rule of thumb according to amino acid and glucose concentrations (Table I). A final glucose concentration of ≥70 g/L should alert for an osmolality of ≥600 mOsm/kg. However, a final glucose concentration <70 g/L, with final amino acid concentration >10 g/L, may not be of reassurance for an osmolality <600 mOsm/L, and in this case the proposed equation may be particularly useful.

The proposed equation can be programmed in hand calculators or in spreadsheets such as *Microsoft Excel* and laid on the desktop of personal computers, allow-

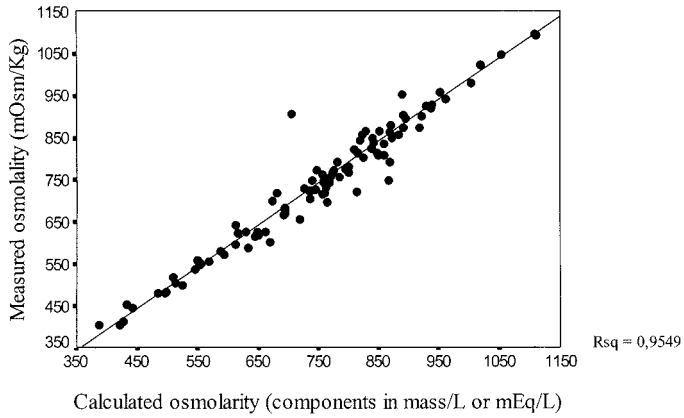

FIG. 2. Prediction of the osmolality of PN solutions by calculated osmolarity (using g/L for glucose and amino acids, mg/L for P, and mEq/L for electrolytes): osmolarity (mOsm/L) = (A × 8) + (G × 7) + (Na × 2) + (P × 0.2) - 50.

ing a quick and easy prediction of osmolalities of routinely prescribed neonatal PN solutions.

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