Association between Magnesium, Calcium, Phosphorus, Copper, and Zinc in Umbilical Cord Plasma and Erythrocytes, and the Gestational Age and Growth Variables of Full-Term Newborns

Michelle Speich, Bernard Bousquet, Jean-Louis Auget, Simone Gelot, and Olivier Laborde

We determined reference values in umbilical cord plasma and erythrocytes for magnesium, total calcium, phosphorus, copper, and zinc, and then calculated correlations and stepwise-regression equations in 66 white full-term newborn infants (35 boys, 31 girls). Only infants meeting certain optimal criteria and benefiting from excellent maternal conditions and uncomplicated pregnancies were included. There were no significant sex-related differences at birth among the variables studied. Gestational age was positively correlated with erythrocyte zinc (P < 0.001), and plasma calcium was positively correlated with erythrocyte copper (P < 0.001). Plasma copper proved to be the most significant variable in the stepwise-regression equation for birth height as the dependent variable. The most significant regressors accounting for birth weight were erythrocyte zinc followed by plasma zinc.

Additional Keyphrases: multivariate analysis · trace elements · reference values

Disorders in mineral element nutrition and metabolism in embryos are potentially mutagenic and teratogenic and may lead to abortion or a wide variety of malformations. Similarly, mineral element disorders later in fetal life may produce growth retardation and various abnormalities (1, 2). Other effects may be latent and be expressed much later in life in the form of neurological and psychological disorders, carcinogenesis, atherogenesis, and even teratogenesis in the subsequent generation (2–6).

Because data on mineral values in newborns are meager in contrast to those for adults, particularly for erythrocytes (which allow an approach to analysis of the intracellular environment), our aim in this paper was to (a) determine reference values in umbilical cord plasma (PI) and erythrocytes (Erc) for magnesium (Pl-Mg, Erc-Mg), calcium (Pl-Ca), phosphorus (Pl-P), copper (Pl-Cu, Erc-Cu), and zinc (Pl-Zn, Erc-Zn) in healthy newborns and (b) search for possible relationships between gestational age and growth variables (birth weight, height, and head circumference) and the concentrations of these minerals.

Materials and Methods

Subjects. We studied 66 white full-term babies (35 boys, 31 girls) born from February to April 1990 in the maternity ward of the University Hospital in Nantes, France. All pregnancies were uncomplicated and resulted in vaginal deliveries after 37 to 42 weeks of gestation. Mothers (ages 19 to 40 years) were healthy and had no history of serious disease. Apgar scores at 1 and 5 min were 10 for all infants. No infant had a congenital malformation.

Assay techniques. Within 5 min of delivery, cord blood specimens were drawn into Venouset Tubes containing lithium heparin (Ref. T206 LH, Code VT 050 HL1; Terumo France, 78181 Saint Quentin en Yvelines Cedex, France) and then, without delay, centrifuged at 3500 × g for 8 min at 10 °C. Immediately afterwards, Mg, Ca, and Zn concentrations were measured by the specific (and reference) method of flame atomic absorption spectrometry (Philips Pye Unicam SP9; Philips, 93002 Bobigny Cedex, France) according to previously described protocols (7). Copper was analyzed by flameless atomic absorption spectrometry (the reference method) with Zeeman effect (Model 3030; Perkin-Elmer, 78054 Saint Quentin en Yvelines Cedex, France) in plasma and erythrocytes diluted 50-fold with demineralized water. Phosphorus was determined by ultraviolet detection (340 nm) of ammonium phosphomolybdate (cat. no. A02477; Biotrol, 75140 Paris Cedex 03, France). For quality control in each series of analyses we used Biotrol 33-plus sera (cat. no. A02270). For all these analytes, intra- and interassay coefficients of variation were 1–2% and 1–3%, respectively. Accuracy ranged between 99% and 102%.

Statistical analysis. We used the Pearson correlation coefficient, stepwise regression, and Student's t-test for comparisons of means according to sex (8). Owing to the 13 variables studied, we used the Bonferroni procedure with the Pearson correlation coefficient to allow adjustment of the significance of each test to 0.001. We used Systat software (Systat Inc., Evanston, IL) to perform these statistical procedures.

Results

Results are given in Tables 1 and 2. Because no statistically significant sex-related differences could be determined for analytes and growth-related variables, we pooled the results for the two groups of newborn infants and considered them as a single population.

After 37 weeks of gestation, the differences in weight (2.530–4.220 kg), height (45–54 cm), and head circum-

---

1 Laboratoire de Biochimie, 2 Laboratoire de Biophysique et Mathématiques, and 3 Laboratoire de Toxicologie et d'Hygiène Industrielle, Faculté de Pharmacie, 1, rue Gaston Veil, B.P. 1024, 44035 Nantes Cedex, France.
4 Hôpital Femme-Enfant, C.H.U., Quai Moncousu, 44035 Nantes Cedex, France.

Received March 29, 1991; accepted October 31, 1991.
ference (31–37 cm) of our infants were sufficiently great to allow calculation of correlations and stepwise regression equations.

The Pearson correlation coefficient (r) proved significant (P < 0.001) whenever its absolute value was greater than the critical value (0.396). The number of weeks of gestation was thus positively correlated with Erc-Zn (r = 0.489), and Pl-Ca was positively correlated with Erc-Cu (r = 0.489). Obviously, there was a significantly positive correlation between gestational age and growth variables (P < 0.001).

The stepwise-regression equations for the 66 newborns were birth weight = 3.460 + 0.009 Erc-Zn − 0.031 Pl-Zn (P = 0.010)—Erc-Zn being the most explicative variable of weight, followed by Pl-Zn—and birth height = 48.265 + 0.201 Pl-Cu (P = 0.074). No regression was found to be significant for head circumference.

Discussion

The specific atomic absorption spectrometry method, which allows easy, precise, and accurate analysis of Mg, Ca, Zn, and Cu, can be applied to erythrocytes, for which very few results have been published to date. However, the different dilutions for use in assays require about 1 mL of blood, which is difficult to obtain except from the umbilical cord. This cord blood corresponds well to infant blood, there being normally no commingling between fetal and maternal circulation. Several recent studies have investigated electrolyte and trace element concentrations in the plasma or serum of newborns (6, 9–17), with results similar to our own reference values. However, very few reports concerning erythrocytes exist, and those known concern only Erc-Zn (18–20). As in our study, no differences with regard to sex have been detected for magnesium (15), copper, or zinc (21).

The most significant regressors accounting for birth weight were Erc-Zn and Pl-Zn. Except for Arumanayagam et al. (22), who found no significant positive correlations between cord Pl-Zn and birth weight, most authors have reported significant positive correlations between birth weight and Pl-Zn (21, 23) or Erc-Zn (20).

Because Zn is an essential component of many enzyme systems implicated in normal cell division and is required for protein synthesis, impairment of these processes may retard fetal growth and reduce birth weight (5, 24–26). Consequently, the negative sign of the Pl-Zn coefficient in our stepwise-regression equation could be attributed to the movement of zinc from plasma toward the intracellular compartment.

Fetal growth and energetics depend strongly on the exchange of nutrients across the placenta, which is also the site of metabolic activity and hormone production. The placenta transports Ca ions actively, making the fetus hypercalcemic relative to the mother. This results in the release of calcitonin and may inhibit secretion of parathyryn, which would be conducive to fetal skeletal formation (9). Fetal Pl-P and Pl-Mg concentrations are also higher than those of the mother (9, 27, 28). Evidence for an active maternal–fetal transfer of Mg across the placenta has recently been presented (29). The Mg gradient is sufficient to protect the fetus from severe maternal Mg deprivation (28).

Physiological changes during pregnancy include decreased Pl-Zn and increased Pl-Cu concentrations. The decrease in Zn reflects a maternal–fetal transfer, an expansion of maternal plasma volume, decreased Zn-binding affinities or transport protein concentrations, and increased Zn requirements or inadequate Zn intakes (19, 30, 31). The increase in Cu can be attributed to increased ceruloplasmin, the result of increased estrogen concentrations (16, 17). At birth, Pl-Zn values in infants are higher and Pl-Cu values lower than those of the mother when pregnant or in nonpregnant women.
The high Pl-Zn concentration may reflect an active transfer of Zn across the placenta (19, 22, 31). The low Pl-Cu concentration may be associated with a low fetal ceruloplasmin content (16, 17). Very little investigation has been devoted to the determination of the erythrocyte concentration of these variables in newborn infants. Fetal ErC-Zn concentrations have been found to be much lower than in adults (7). The fact that ErC-Zn is predominantly associated with the carbonic anhydrase (EC 1.4.2.1) enzyme system may indicate that lower ErC-Zn values in neonates correspond to relatively low concentrations of carbonic anhydrase (2, 5, 19). We noted a positive correlation between ErC-Cu and Pl-Ca (P <0.001) not previously reported. The relationships between metabolic bone diseases and low serum Cu concentrations in infants, recently suggested by Koo et al. (32), have not yet been confirmed.

There were no significantly sex-related differences at birth among the variables studied. The most significant variable related to gestational age and birth weight determined from our correlation and stepwise-regression calculations was ErC-Zn. These neonatal reference values will be used in further comparative studies of newborns with various pathologies or whose mothers have various diseases.

We thank Nicole Robinet-Le Gall and François Dominguez for their technical assistance in the copper and phosphorus assays, respectively.

References