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ANALYSES OF SERUM VITAMIN D – BINDING PROTEIN, CERULOPLASMIN AND COPPER LEVELS IN PRETERM INFANTS*

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SUMMARY: Paşaoğlu H, Kurtoğlu S, Muhtaroğlu S. (Departments of Biochemistry and Pediatrics, Erciyes University Faculty of Medicine, Kayseri, Turkey). Analyses of serum vitamin D-binding protein, ceruloplasmin and copper levels in preterm infants. Turk J Pediatr 34: 225-230, 1992.

The cord blood specimens of 12 preterm and 20 term babies were investigated. We determined serum calcium (Ca), phosphorus (P), magnesium (Mg), vitamin-D binding protein (DBP), ceruloplasmin (Cp) and copper (Cu) levels in two groups. We found that Ca, P, and MG levels of cord sera did not differ between the groups ($p > 0.05$), but DBP, Cp and Cu values showed a significant decrease in the preterm group ($p < 0.05$). The Cu and Cp values of the preterm infants correlated with those of the term infants.
Key words: preterm baby, DBP, Cp, Cu.

It has been documented that early neonatal hypocalcemia is a common occurrence in the first week of life in preterm infants[1], while absorption and activation of vitamin D are observed 24 hours after birth in preterm infants born after 31 weeks of gestation. Early neonatal hypocalcemia is unlikely to be caused either by impairment of parathyroid hormone secretion or vitamin D activation[2]. Vitamin D and its metabolites circulate in the blood bound to a specific vitamin D-binding protein (DBP). Vitamin D-binding protein is similar to other binding proteins, such as ceruloplasmin (Cp), in that it is produced in the liver[3,4]. During the last trimester of pregnancy, most of the zinc (Zn) and copper (Cu) is transported through the placenta to the developing fetus[5]. Copper deficiency has been found in preterm infants[6-8]. Copper is a trace element that plays an important role in many metabolic processes related to body growth, the blood system, and bone mineralization[7,9]. Recently attention has been focused on calcium (Ca), phosphorus (P), Zn, and Cu nutrition in newborns, and on its relation to physical growth and dietary intake[10-12].

In this study, we examined the DBP, Cp, Cu, Ca, P, and magnesium (Mg) levels in cord blood of preterm and term infants to determine liver maturity and mineral values in preterm infants.

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Material and Methods

Cord blood specimens were obtained from 20 term and 12 preterm infants who were born in the Department of Obstetrics at Erciyes University Faculty of Medicine from May to August. Since Specker et al[13] reported seasonal differences in infants who were less than six months of age, we decided to conduct our study in the summer.

Gestational ages were determined using the scoring system devised by Dubowitz et al[14], which ranged from 26 to 35 weeks (mean ± SD; 33.5 ± 1.5) The mean birth weight of the preterm group was 2221.7 ± 125.2 g (range 750 to 2500 g).

Cord serum Ca and P concentrations were determined using the Encore standard Autoanalyzer (Baker, GB), and Mg and Cu levels were measured by atomic absorption spectrophotometry (Hitachi Z-8000)[15]. Vitamin D-binding protein values were assessed by the single radial immunodiffusion technique according to the method of Bouillon et al[16].

DPB antiserum and standard were provided by Prof. Bouillon of Leuven, Belgium. Cp levels were measured by the p-phenylenediamine oxidase method[17].

All data were expressed as a mean ± SD. For statistical analyses, the Student's *t* test and regression analysis were used.

Results

The cord serum DBP, Ca, P, Mg, Cu, Cp values of the preterm and term groups are listed in Table I.

The serum DBP, Cp and Cu levels of the preterm group were found to be significantly decreased, but the Ca, P, and Mg values did not differ between the groups.

Table I: Cord Serum DBP, Ca, P, Mg, Cu and Cp Levels in Preterm and Term Infants

	Preterm	Term	
n	12	20	
M/F	8/4	10/10	P
	$\bar{x} \pm SD$	$\bar{x} \pm SD$	
DBP (mg/l)	268 ± 30	301 ± 45	$p < 0.02$
Ca (mg/dl)	10.0 ± 0.6	10.3 ± 0.7	$p > 0.05$
P (mg/dl)	4.6 ± 1.3	4.8 ± 0.7	$p > 0.05$
Mg (mg/dl)	2.3 ± 0.6	2.2 ± 0.4	$p > 0.05$
Cu (ug/dl)	37.5 ± 10.9	49.8 ± 14.3	$p < 0.02$
Cp (mg/dl)	14.5 ± 5.8	20.6 ± 6.4	$p < 0.01$

In the preterm infant samples, the correlation found between the serum Cu and Cp values was $n = 12$, $r = 0.674$, $p < 0.05$, while the correlation in term infants was $r = 0.78$, $p < 0.001$.

Discussion

Vitamin D-binding protein is actively synthesized in fetal liver after the 10th gestational week, and its prenatal serum level is half that of the maternal level[18]. It has been reported that DBP concentrations are at normal adult values in cord blood of term infants, but that preterm infants have low serum DBP concentrations[19], a finding which has been confirmed by other investigators[20].

Lichtenstein et al[21] have demonstrated that starting from birth to 18 months of age, DBP concentrations increased with age. Workers have found that formula-fed infants have higher serum concentrations of all measured vitamin D metabolites and DBP than breast-fed infants[21].

Hillman et al[22] have reported that DBP values increased linearly from 29.7 ± 2.5 to 40 weeks of gestational age. Auconi et al[23] have reported that the mean value of DBP serum levels steadily increases from the 32nd to the 35th week of gestation. This pattern of increase is similar to the patterns of serum concentrations of a number of proteins produced in the liver such as Cp, and therefore Cu[24,25].

Our data demonstrated that DBP levels of preterm babies are lower than those observed in term babies. These results are similar to reports in the literature[22,23].

In our study, we found no difference in the cord serum Ca, P and Mg levels between the preterm and term infants, although the Cu and Cp levels were found to be decreased in the preterm group of infants. Studies have demonstated the same results in cord blood[2,4]. However, when compared with cord blood levels, serum calcium concentrations were found to decrease significantly during the first 24 hours after birth and remained low until the forth day. In addition, serum 25-OH D levels are found to decrease in preterm infants. Hillman[24] has shown that in 57 very early preterm infants studied, serum Cu concentrations remained low for the first 9-12 weeks of postnatal life. He suggested that the ability to increase serum Cu and Cp concentrations is a maturational process, with less mature infants having longer delays.

We examined the Cu-Cp correlation both in preterm and term infants, and found our results to be similar to Hillman's findings[24].

The concentration of copper is significantly higher in term infants than in adults, and it is believed that low copper and ceruloplasmin values in newborn infants reflect an immaturity of the ceruloplasmin synthetic mechanism rather than copper deficiency[26].

Both term and preterm infants begin life with low serum Cu and Cp values. Term infants increase their copper concentration to adult levels by increasing Cp production in mobilizing liver stores by one month of age[24]. Copper concentration in the liver of preterm infants does not decrease, but total stores are limited by a smaller liver size[5, 27]. If sufficient quantities of Cu are not provided in a bioavailable form in postnatal life, a deficient state may develop in preterm infants[8].

Infants of very low birth weight are at risk of developing many serious nutritional deficiencies including Cu deficiency. Copper deficiency of premature infants results in bone changes, neutropenia, anemia and poor weight gain. We recommend that facilities for measurement of plasma Cu and Cp be made available to all neonatal units, and that it should be considered as part of routine investigations in the class of infants mentioned above. It is important that early diagnosis is arrived at, and that treatment is administered before major clinical features appear.

In addition to Cu, vitamin D supplementation is important for the preterm infant.

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