A COMPARATIVE STUDY OF CORD SERUM COPPER IN FULLTERM AND PRETERM INFANTS WITH MATERNAL - INFANT RELATIONSHIP

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ABSTRACT

The study was conducted on 43 newborn infants (23 full term and 20 preterm) and their mothers in Basrah Maternity and Children Hospital over a period of six months (December 1998 till May 1999) to determine the cord serum copper levels at birth in both full term and preterm infants, and to study the relationship between these levels and the corresponding levels in their mothers. Compared to normal full term infants, preterm infants showed significantly lower levels of cord serum copper. Maternal levels of serum copper at delivery were markedly higher than the corresponding levels of cord serum copper in the two groups of newborn infants.

INTRODUCTION

Copper is an essential trace element[1]. Its possible significance in human metabolism was not appreciated until 1928, when Hart et al., showed that copper is an essential nutrient for the rat[2]. Copper is involved in many vital processes. Copper as a constituent of many enzymes, is involved in energy production via oxidative phosophorylation, in the protection of cell membranes against oxidative damage, in the oxidation of iron released from storage, in eryrthropoietin synthesis, and in cerebral protein and myelin deposition[3,4]. In plasma copper is found in four fractions: *Ceruloplasmin*, which is synthesized in the liver and is released into the circulation, where it accounts for the majority of the plasma copper (carries 90% of the copper present in plasma)[2]. Another fraction is *Transcuprein*, which is the predominant vehicle of copper transport to the liver in the portal circulation[3] *Albumin* carries 10% of the plasma, copper, it donates its copper to tissues more readily than ceruloplasmin[1], and the last fraction includes *various low-molecular weight components*[3]. Large amounts of copper are deposited in fetal liver during the third trimester[3], the liver of term infant contains a copper concentration 10-20 fold greater than that in the liver of adult[3]. Serum levels of copper and ceruloplasmin are low at birth and remain low for several weeks in preterm infants[5]. Levels rise however, as ceruloplasmin synthesis begins between 6^{th} and 12^{th} postnatal weeks, varying with the gestational age of the infants[3], suggesting that the ability to increase serum copper and ceruloplasmin concentration is a maturational process, with less mature infants having longer delays[6]. Copper deficiency was reported in infants recovering from protein-energy malnutrition and in patients receiving total parenteral nutrition[3]. Because premature infants have reduced copper stores, and have increased copper demands for rapid growth, the potential for copper deficiency is significant[6]. The principle features of copper syndrome are *haematological changes* mainly neutropenia and anaemia[5], *neurologic findings* like hypotonia psychomotor retardation, apnea, ataxia and pseudoparalysis[3,5]. Other clinical features include *depigmentation of the skin and hair, failure to thrive, diarrhoea and odema*[2,3]. *Blood vessels rupture* may occur[3] and also prominent scalp veins in palpable periosteal depressions[2]. *Roentgenographic changes* include osteoporosis, blurring and cupping of metaphysis, subperiosteal new bone formation and fractures[2,5]. Transient vitamin D resistant rickets also may occur[7].

The present study is an effort to determine the levels of cord serum copper in normal full term and preterm infants and the relationship between the levels of serum copper in the mothers at delivery and the corresponding cord serum copper levels in the above two groups of newborn infants.

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PATIENTS AND METHODS

The study was performed at Basrah Maternity and Children Hospital between December 1998 to May 1999 on 43 mothers and their newborn infants who were divided into two groups:

Group I: *included 23 normal full term infants (13 males and 10 females). Their birth weight ranged from 2600-4300gm and their gestational age from 38-42 weeks.*

Group II: *included 20 preterm infants (10 males and 10 females). Their birth weight ranged from 1000-2200 gm and their gestational age from 28-36 weeks.*

The gestational age was calculated according to the date of the last menstrual period and confirmed by clinical examination using the Dubowitz scoring system[5]. A thorough clinical examination of every infant was carried out and they were all selected to be free from any affection whether congenital or acquired that might derange the results. The age of the mothers ranged from 17-38 years and their parity from 0-7. Studied mothers have received antenatal care and they were all clinically healthy. Blood samples were taken from the mothers (2ml of venous blood) during the second stage of labour and from the cord immediately after clamping and before delivery of the placenta. Blood was analyzed for serum copper using kits from Randox Laboratories Ltd., that is based on calorimetric methods[9]. Serum copper values were expressed as μg/dl.

Statistical analysis:

Data were expressed as the (mean ± S.D.), "t" test was carried out to determine the relative importance of various variables, P value less than 0.05 was considered as statistically significant.

RESULTS

A total of 43 newborn infants (23 full term and 20 preterm) and their mothers were included in this study to assess the serum copper level. Twenty-three of the newborn infants were males (13 full term and 10 preterm) and 20 were females (10 full term and 10 preterm) (Table-1). Regarding serum copper the study demonstrated that the level in preterm infants was significantly lower (p<0.01) than that in full term infants (Table-2). The study had shown that serum copper in preterm infants significantly increased with increasing gestational age (P<0.01) (Table-3). In relation to maternal-infant relationship of serum copper the study had shown that the mean serum copper level in mothers of normal full term infants and also mothers of preterm infants was significantly higher (P<0.01) than the mean level of cord serum copper of their corresponding infants (Table-4).

Table 1. ***Distribution of cases according to sex and gestational age.***

Group	Male		Female		Total	
	No.	%	No.	%	No.	%
Full-term	13	56	10	50	23	54
Preterm	10	44	10	50	20	46
Total	23	100	20	100	43	100

Table 2. ***Cord serum copper (μg/dl) of full term and preterm infants (mean ±SD).***

Group	Cord serum copper (±μg/dl)	P-value
Full-term infants (n)=23	45.94 ± 13.57	P<0.01
Preterm infants (n) = 20	29.53 ± 6.84	

Table 3. ***Cord serum copper (μg/dl) of preterm infants according to gestational age (Mean ± SD).***

Group	Cord serum copper (μg/dl)
28-30 weeks (n=5) 31-33 weeks (n=8) 34-36 weeks (n=7)	22.25 ± 3.20 28.16 ± 1.16 37 ± 5.38

Table 4. ***Cord serum copper (μg/dl) of full-term Infants, preterm infants and their corresponding mothers.***

Group	Serum copper (μg/dl)	P-value
Full term infants (n=23) Mothers of full term infants (n=23)	45..94 ± 13.57 205.36 ± 41.25	P<0.01
Preterm infants (n=20) Mothers of preterm infants (n=20)	29.53 ± 6.84 194.93 ± 19.91	P <0.01

DISCUSSION

The present study has thrown a light on the levels of cord serum copper in both full term and preterm infants and also on the relationship between these levels and the corresponding levels in their mothers. In the present study it was observed that at birth the level of cord serum copper in preterm infants was significantly lower than that in full term infants (Table-2). Our results were comparable to that reported in previous studies that showed similarly low serum copper concentration in preterm infants at birth[6,9-11]. This may be explained by that prematurity due to short period of gestation diminishes the transport of free copper from the mother to fetus to reach equilibrium[12]. In addition to this, diminished synthesis of ceruloplasmin in preterm infants due to immatrurity of their liver may offer another explanation to the low level of cord serum copper in these infants[4,6,12,13}. Ninety percent of the plasma copper is present as ceruloplasmin[2]. Diminished ability of preterm infants to mobilize copper from their liver together with diminished total stores of copper in their liver due to their small liver size may explain similarly the lower cord serum copper in preterm infants[14]. In the present study it was also found that the mean cord serum copper level of preterm infants at birth increases with increasing gestational age (Table-3). This confirms the observations made by other workers[6,14]. The proposed explanation for these observations is the increased accumulation of copper in the liver of human fetus with increasing gestational age[2]. In the present study it was also found that the mean levels of serum copper in the mothers of both premature and term infants at delivery was markedly higher than the corresponding levels of their infants (Table-4). These observations confirm a previous report regarding a large difference between maternal and cord serum copper levels at birth[6,13,15]. A possible explanation for this difference is that serum ceruloplasmin levels, together with the levels of other globulines, are known to rise during pregnancy due to increased estrogen level, this rise is also reflected as an increase in serum copper level. In addition to that, because ceruloplasmin is not transported across the placenta, it is only the small part of free copper which is diffusible and is in equilibrium on both the maternal and fetal sides of the placenta[12]. From this study we conclude that there is:

1- *A significant low cord serum copper levels in preterm compared to full term infants.*

2- *A considerable feto-maternal difference regarding serum copper levels.*

RECOMMENDATIONS

A serial measurements of serum copper concentrations is needed in premature infants particularly those who have haematologic or bone abnormalities to look for the possibility of copper deficiency and also to judge the supplementation of this element in these infants.

Further study is needed to determine the spectrum of cord serum copper in small for gestational age infants (SGA).

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