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Short Communication

Results of a Study to Detect the Effects on Neonates of Copper and Zinc Deficiency During Pregnancy

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Trace element deficiency during pregnancy is hypothesized to occur in humans and to produce neonatal malformations, but few large-scale studies have been performed. To investigate such deficiencies we measured zinc and copper in the serum of 540 mothers and newborns at delivery, looking for an association between decrease of serum level and newborn malformations.

MATERIALS AND METHODS

Blood was collected in trace-element free polystyrene tubes at delivery from women and their newborn (cord blood). Zinc was measured in serum by flame atomic absorption after 1:5 dilution of serum with deionized water, and copper by flameless atomic absorption (graphite furnace HGA 500 connected to a 560 Perkin Elmer spectrophotometer) after 1:10 dilution with deionized water.

RESULTS

We calculated corrected normal values after excluding all values out of two standard deviations (SD) from general mean (results are in Table 1). Distribution of values for all mothers and children show us that all parameters have a Gaussian distribution, except copper in cord blood. We therefore took a lower limit of three SDs except for copper in cord blood (two SDs). Among 26 newborns under this limit, seven presented some malformations but only two had severe neural malformations. It is worth noting that we found three newborns with severe jaundice and low levels of copper in cord blood, and their mothers all had abnormally high levels of zinc.

Of 540 deliveries we found a total of 13 malformed children. They all presented very mild malformations except the two major neural malformations previously quoted, but the mean of mother's zinc and of copper in cord blood were abnormal (Table 1).

DISCUSSION

For many years the attention of researchers has been attracted by the teratogenic affects of maternal trace element deficiencies in animals (Hurley, 1976, 1981*a*, 1981*b*; Shaw, 1980). The more dramatic effects are obtained with zinc, copper and maganese; deficiencies

Table 1 Zinc and copper levels of mothers and children in normal and pathological deliveries

	Zinc		*Copper*	
	Mother	*Children*	*Mother*	*Children*
Non pregnant female: normal value (μg/dl)(mean ± SD)	103 ± 12		140 ± 34	
Normal deliveries (μg/dl)(mean ± SD)	84 ± 14	126 ± 24	262 ± 40	55 ± 19
Lower limit (μg/dl)	43	53	140	18
Total newborns under limit (No.)	6	8	3	9
Malformed newborns under limit (No.)	2	3	0	2
Malformations	Mild hip deformations Hydrocephalus	Small weight (2) Mild hip deformations	0	Myelomeningocelus Mild bone deformations
All malformations (n = 13)(mean ± SD)	63 ± 25	132 ± 23	256 ± 60	80 ± 16
Student's t-test	$p<0.001$	$p = 0.40$	$p = 0.7$	$p<0.001$

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create brain abnormalities, often neural-tube defects, skeletal abnormalities and lung malformations. Copper deficiencies cause brain abnormalities with synthesis of an abnormal myelin, transparent and brittle bones, and lung and heart malformations. Manganese deficiencies cause ataxia and skeletal malformations.

In contrast there is little documentation on the effects of such deficiencies during human pregnancy, but many studies (Hambridge *et al.*, 1975; Bergman *et al.*, 1980; Cavdar *et al.*, 1980; Sever and Emanuel, 1973; Jameson, 1976) seemed to point to a link between zinc deficiencies and neural malformation. In our study we found that the only two severely malformed newborns presented an abnormal trace-element status. One was still-born from cousin parents, and presented hydrocephalus and heart and lung malformations. His karyotype was normal, but his mother had a very low level of zinc (43 μg/dl). The other child, born from cousin parents, had an open myelomeningocele that the parents did not wish to be treated, and that evolved to hydrocephalus (death at 25 days). The mother and child presented a normal zinc status but the child had a low level of copper in cord blood (18 μg/dl).

CONCLUSION

Our study shows a link between malformation and zinc deficiency in mother, or copper deficiency in newborn, but this is not a direct relationship to levels under a certain limit. We know that the level of copper or zinc in serum is not a good index of trace element deficiencies, and is disturbed by hormonal changes. Zinc deficiencies may thus be transitory and the first months of pregnancy are most dangerous. Unfortunately in our study we would not have detected such a deficiency at the beginning of pregnancy.

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