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Short Communication

Role of Zinc, Copper and Manganese Concentration in Neural Tube Defects

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Trace minerals are required by the body in minute quantities ranging from as little microgram to milligram per day. The trace elements known to be essential for humans and unquestionably associated with deficiency system. Zinc is a component of all cells; it is needed for the growth and repair of tissues and is a cofactor for at least 70 different enzymes (Baumgartner, 1993). There is experimental evidences for zinc deficiency as a teratogenic agent and in humans the high rates of neural tube defects (NTD) in some regions where zinc deficiency is common (Hurley, 1981; Sever, 1989). In animals zinc deficiency has been shown to cause central nervous system defects (Keen and Hurley, 1989). It is well known that there are interactions between zinc and other trace minerals. Normal levels of these and good relation between them are factors conditioning human health (Janicki, 1991). The present study aims at assessing blood, serum zinc, copper and manganese levels and zinc/copper, zinc/manganese ratios of mother and their babies having NTD.

Blood samples of the mothers in the age group of 18-35 years with NTD babies were included in the study. All the mothers come from the low socioeconomic profile. Women with normal babies at the same age group were included as controls. The venous blood (5.0 ml each) from all newborns and their mothers was drawn from an antecubital vein, using stainless steel needles (disposable syringes) and collected in trace element free plastic vials. All necessary precautions were taken to avoid contamination. After one hour of collection, the blood was centrifuged and the clear serum was transferred to plastic vials. The sera were stored frozen at-20°C until analyzed.

The blood from each case was divided into three groups. In group (I) whole blood, in group (II) blood serum and in group (III) packed cell mass was subjected for extraction of zinc. All the samples were digested in long necked round bottom flasks with triple acid (conc. HNO_3, 70% perchloric acid and conc. H_2So_4, 10:3:1). This process was executed by heating the

Table 1. Trace element levels in normal and NTD mothers (Mean±SD).

	Zn (µg/ml)	Cu (µg/ml)	Mn (µg/ml)	Zn/Cu (µg/ml)	Zn/Mn (µg/ml)
In blood					
NTD mother	14.56±1.34 (5.99)	1.11±0.034 (0.15)	1.61±0.314 (1.4)	18.12±0.99 (14.18)	26.88±2.0 (28.8)
Control mother	24.15±2.95 (13.2)	1.32±0.053 (0.24)	0.904±0.057 (0.26)	10.50±0.35 (5.03)	18.19±0.94 (13.5)
In serum					
NTD mother	0.606±0.016 (0.02)	1.09±0.086 (0.38)	0.097±0.013 (0.06)	1.39±0.13 (1.8)	26.08±43.7
Control mother	0.719±0.035 (0.16)	1.45±0.065 (0.29)	0.054±0.009 (0.04)	0.53±0.01 (0.27)	23.94±25.93
	p<0.05	p<0.05	p<0.05	P<0.001	p<0.001

Table 2. Trace element levels in normal and NTD newborns (Mean±SD).

	Zn (µg/ml)	Cu (µg/ml)	Mn (µg/ml)	Zn/Cu (µg/ml)	Zn/Mn (µg/ml)
In blood					
NTD newborns	15.65±3.18 (14.26)	1.039±0.096 (0.4)	1.29±0.151 (0.67)	17.33±0.94 (13.5)	17.46±1.2 (17.3)
Normal newborns	28.04±1.11 (4.9)	1.505±0.78 (0.35)	0.856±0.64 (0.29)	24.08±0.41 (5.97)	35.60±0.74 (10.59
In serum					
NTD newborns	0.556±0.079 (0.35)	0.59±0.055 (0.25)	0.278±0.04 (0.16)	0.77±0.59	63.66±173.54
Normal newborns	0.596±0.08 (0.40)	0.784±0.033 (0.15)	0.111±0.015 (0.07)	0.65±0.52	16.98±22.67
	p<0.05	p<0.05	p<0.05	P<0.001	p<0.001

contents till most of the triple acid mixture evaporated from the flask. The contents of each flask were then washed with triple distilled water and were stored in plastic vials at 4°C for further analysis. The zinc levels as µg/ml were determined on GBC 932 spectrophotometer by fluorometery.

All the data were given as arithmetic means, SD, SEM and ranges. The 95% confidence intervals (CI) for the population means were also shown. T-test was used to compare the trace mineral levels of the subjects. The mean blood, serum zinc, copper and manganese concentration in control mothers and their babies and those with NTD is shown in tables 1 and 2. NTD mothers and their babies had significantly lower zinc level than those of control group ($p<0.05$). Both the tables also represent the Zn/Cu and Zn/Mn ratios of both the groups. This ratio varies significantly.

The actual etiology of NTD is still unknown. Maternal zinc status was proposed as a possible causative factor. Zinc deficiency in humans leads to impaired absorption of dietary folate and involved in the metabolism of anti-epileptic drug. Either reports on the association between congenital malformation and maternal deficiency or high rates of NTD occurrence observed in the countries with prevalence of zinc deficiency and prevention of maternal complications with zinc supplementation give strong evidence for this possible correlation between dietary zinc deficiency and NTDs (Cavdar *et al.*, 1988; 1991; Akar *et al.*, 1991; Dincer and Akar, 1995).

Zinc concentration in blood, plasma and serum of the mother having NTD babies and their neonates are lower than those in control who gave birth to normal babies (Rajeev, 2000; Srinivas *et al.*, 2001; Golalipour *et al.,* 2006; Zeyrek *et al*., 2009; Dey *et al.,* 2010). In the present study we aimed at investigating the blood, serum zinc, copper and manganese levels and

Zn/Cu and Zn/Mn ratios of NTD mothers and their babies. It is interesting to say that all the values differ significantly. Our result supports the earlier studies of Cavdar *et al.* (1988), Dincer and Akar (1995), Golalipour *et al.* (2006), Zeyrek *et al*. (2009) and Dey *et al.* (2010).

We can conclude from our data that decreased maternal blood, serum analysis is important for the assessing of the maternal Zn status and it is reasonable to propose that if Zn plays a significant role during the embryogenesis, the existence of zinc deficiency may be important especially for the women with NTD.

We also recommended that additional attentions be paid to the mechanism of neural tube closure and the potential role of dietary Zn in the absorption and metabolism and their effects on the neural tube.

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