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Department of Paediatric Propedeutics, Department of Neonates,
Infants Pathology and Cardiology, Medical University of Lublin

ARTUR KOŚCIESZA, BEATA KULIK-RECHBERGER,
RENATA JAWNIAK, WANDA FURMAGA-JABŁOŃSKA

Zinc and copper concentrations in the cerebrospinal fluid in infants with neural tube defects

Neural tube defects (NTDs), resulting from failure of the neural tube to close during the fourth week of embryogenesis, are the most common birth defects of the central nervous system. Neural tube malformations ranges from minor defects of the vertebral arch (*spina bifida occulta*) to severe, clinically important types involving protrusion of the brain or spinal cord and meninges through the cranial or vertebral arch defect. Depending on the level of the lesion, interruption of the spinal cord causes paralysis of the legs, incontinence of urine and faeces, anaesthesia of the skin and abnormalities of the hips, knees and feets. The additional abnormalities often seen in children with NTDs are hydrocephalus (approx. 85–90% of babies) and the Arnold-Chairi type II malformations.

The aetiology of the neural tube defects is multifactorial. In addition to genetic factors, environmental influences are also important. Parental age, education, occupation, socioeconomic status, maternal health and nutritional status have been explored as potential risk factors, but no definitive conclusions have been reached (4).

The trace elements – zinc and copper are additional nutrients, essential for fetal growth and development and required for optimal central nervous system function. They are needed to activate and stabilize enzymes, such as a superoxide dismutase, metalloproteases and protein kinases (8). Inadequate maternal zinc intake is associated with increased risk of NTDs, but it is still unclear how trace elements are involved in the pathogenesis of NTDs (7).

In our study we tried to evaluate the zinc and copper concentrations in cerebrospinal fluid (CSF) in infants with neural tube defects.

MATERIAL AND METHODS

The study was conducted at the University Children's Hospital in Lublin. Seventeen infants with neural tube defects and hydrocephalus constituted the study group (14 had meningomyelocele and 3 encephalocele). Cerebrospinal fluid samples were collected, when ventriculoperitoneal shunt was performed. The control group comprised 20 infants treated in the Department of Neonates', Infants Pathology and Cardiology due to the infections, 12 suffered middle ear infections, 5 suffered pneumonia and 3 urinary tract infections. They underwent a lumbar puncture for the exclusion of bacterial meningitis. The parameters of the cerebrospinal fluid in both groups were normal. Preterms and infants with meningitis, intraventricular hemorrhage or seizures were excluded from the study. Table 1 gives the descriptive data for the groups.

Table 1. The description of the investigated groups of infants

		Study group (n = 17)	Control group (n = 20)
Weight (kg)		2.95–5.18	3.68–9.12
Head circumference (cm)		39–45	38–48
Intracranial pressure (mm H_2O)		140–180	-
Sex	boys	6	8
	girls	11	12
Feeding	breast-fed	2	14
	formula-fed	15	6
Place of living	city	6	10
	town	11	10

The concentrations of zinc and copper in cerebrospinal fluid were measured using flame atomic absorption spectroscopy method (AAS). The distribution of studied data sets were checked up by Kolmogorov-Smirnov test. Statistical analysis was performed with Levene test for equality of variances and t – test for two independent samples. 2-Tailed $P < 0.05$ was regarded as statistically significant.

RESULTS

The concentrations of zinc and copper in cerebrospinal fluid in infants with neural tube defects were higher than in control group, but the difference was not statistically significant (Table 2).

Table 2. Comparison of zinc and copper concentrations in cerebrospinal fluid (CSF) in infants with neural tube defects (NTDs) and in control group

	Concentration of copper in CSF (μg/dl)	Concentration of zinc in CSF (μg/dl)
Infants with NTDs (n = 17)	8.50 ± 8.42	6.36 ± 6.04
Controls (n = 20)	6.41 ± 4.95	3.85 ± 2.77
Significance	not significant	not significant

DISCUSSION

Advances in research to uncover the molecular basis of neural tube defects is enhanced by knowledge of the genetic and environmental factors involved in the etiology of the disease. An important role in morphological growth of the fetus play trace elements like zinc and copper. Zinc is required for cell division, development and differentiation. As a co-factor for many enzymes it may be protective against congenital malformations. A number of enzymes require also copper, and its deficiency results in inadequate collagen cross-linking and diminished tensile strength of tissues. Zinc and copper deficiencies have been reported to result in structural and biochemical abnormalities in the fetus, including neural tube defects (1, 5). Results are not consistent. Among results that showed an association between NTDs and zinc deficiency we can cite a study conducted by Carrillo-Ponce and co-authors (1). They observed that serum zinc concentration in children with NTDs was lower than in the control group. Srinivas and colleagues (6) found a relation between NTD and low zinc levels in

the hair in mothers and children with NTDs without any differences in the serum zinc concentration. Moreover Cengiz and colleagues (2) noticed that mid-pregnancy serum zinc concentration is lower in women with fetuses with confirmed neural tube defects. They also reported height serum copper level in cases when compared to controls. These results are not consistent with results of McMichael and co-authors (3). They found that mean maternal serum zinc concentration was higher in cases than controls but there were no case-control differences for serum copper concentrations. Maybe some diversity of finding are results from different sources and methods to assess zinc and copper concentration. In the present study, we evaluated concentrations of zinc and copper in cerebrospinal fluid (we did not find any similar studies published previously). There were no significant differences between infants with NTDs and infants from control group but it is not possible to rule out that investigated trace elements take part in pathogenesis of NTDs. More infants with neural tubes defects were formula-fed than in control group, which rather cannot influence zinc and copper concentrations in the cerebrospinal fluid (9). The etiology of NTDs cannot be expelling with one strict etiologic mechanism. In our opinion, trace metals and molecular pathways they regulate, may be valuable targets for the development of better understanding of the cellular and molecular mechanisms that lead to neural tube defects.

CONCLUSIONS

The concentrations of zinc and copper in cerebrospinal fluid in infants with neural tube defects are similar to those in control group. Further studies are needed to elucidate the possible concern of the trace metals in etiology of neural tube defects.

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SUMMARY

Zinc and copper deficiencies have been reported to result in structural and biochemical abnormalities in the fetus, including neural tube defects. Seventeen infants constituted the study group. Cerebrospinal fluid samples were collected, when ventriculoperitoneal shunt was performed. The control group comprised 20 infants that underwent a lumbar puncture for the exclusion of bacterial meningitis. The concentrations of zinc and copper were measured using flame atomic absorption spectroscopy method. Cerebrospinal fluid zinc and copper concentrations in infants with neural tube defects were similar to those in control group. Further studies are needed to elucidate the possible concern of the trace metals in etiology of neural tube defects.

Stężenie cynku i miedzi w płynie mózgowo-rdzeniowym u niemowląt z wadą cewy nerwowej

Niedobory cynku i miedzi uważane są za przyczyny strukturalnych i biochemicznych nieprawidłowości u płodu, w tym zaburzeń rozwoju cewy nerwowej. Grupę badaną stanowiło 17 niemowląt, u których płyn mózgowo-rdzeniowy pobierany był podczas zakładania połączenia komorowo-otrzewnowego. Grupę kontrolną tworzyło 20 niemowląt, u których pobierano płyn celem wykluczenia bakteryjnego zapalenia opon mózgowo-rdzeniowych. Stężenie cynku i miedzi badano metodą płomieniową absorpcyjnej spektroskopii atomowej. Wykazano, że stężenia cynku i miedzi u dzieci z wadami nie różnią się istotnie od stężeń cynku i miedzi u zdrowych niemowląt.