RELATIONSHIP BETWEEN PLASMA LEVELS OF ZINC AND GROWTH OF CHILDREN UNDER THE AGE OF THREE

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Abstract
Background
Nutrition influences the health and growth of children. Improper alimentation in young children causes growth disturbances.
Methods
In cross-sectional studies (2009-2011), data on weight, height and plasma concentration of zinc were collected for 98 children (<3 years), from Bihor county, Romania. A total of 96 recruited children were available for analysis. The colorimetric method with Br-PAPS final point was used for zinc level.
Results
Zinc level was positive correlated with weight-for-age z-scores ($r=0.41$, $p<0.001$), height-for-age z-scores ($r=0.59$, $p<0.001$) and not correlated with weight-for-height z-scores ($r=0.19$, $p=0.063$).
Conclusion
In children under the age of 3, plasma values of zinc are influenced by weight, height and not influenced by weight.

Key words: zinc, children, growth, alimentation.

INTRODUCTION

Zinc is a micronutrient whose multiple roles are still not fully known. The scientific literature of the past fifty years has recognized three main classes of functions of the zinc ion: catalytic, structural, and regulator functions (Szewczyk, 2013)

Due to the numerous roles exercised by the zinc ion, zinc deficit causes dysfunctions in the enzymatic and immune systems, as well as failures of cellular growth and development. In consequence, clinic signs of chronic zinc deficit are anorexia, growth retardation, alopecia, lethargy, teenage male hypogonadism, rough teguments, delayed wound healing, skin lesions, neurosensory disorders, hepatosplenomegaly, recurrent infections, behavioral changes, neurological impairment, endocrine dysfunctions and death (in severe forms of acrodermatitis enteropathica) (Ackland, Michalczyk, 2006; Bahl, 1998; John et al., 2010).

In the human organism, zinc is found in a very small quantity. When supplemented, it does not form deposits in the body. As a result, there is a constant need for zinc intake through alimentation. The alimentation of children influences their health and growth. Improper nutrition in young children disrupts growth, due to an inadequate intake of micronutrients. Natural sources of zinc are aliments rich in animal protein, which are usually expensive, often inaccessible, especially for children from communities with a low socioeconomic status and from developing countries. The lack of zinc-rich aliments in these regions has had as a result the emergence of zinc deficiencies. When dealing with this deficiency, the most vulnerable group is represented by children, whose bodies are still developing.

Our research aimed to evaluate the relationship between plasma zinc levels and anthropometric indices.

MATERIAL AND METHODS

The study covered the time span between January 2009 and December 2011 and focused on a group of 98 children (aged 0-3 years) from Bihor county, Romania. The group included healthy children who, during the period of the study, underwent blood tests performed through the hospital laboratory service. The tests were part of the routine health screening performed before entering nursery/kindergarten, patient requested tests, or mandatory tests performed two years after an incident of acute viral hepatitis A.

Patients belonging to any of the following groups have been excluded from the study: patients with signs and symptoms suggestive of disease at the moment of examination, patients with a recorded disease in the past 3 months, those who previously underwent therapies with zinc, calcium, copper, iron, laxatives, magnesium-containing anti-acids, and patients who lacked parents' signatures for participating to the study.

The study was approved by the Hospital Ethics Committee in accordance with the Helsinki Declaration 1975 (6^{th} revision, 2008). All the parents gave their consent for the patients included in the study.

The size of the sample group of children included in the study was calculated in rapport with the total number of children under the age of three in Bihor county during the period of the study. The size of the sample population is of minimum 96 for a population of 32.420 children (according to the Bihor County Statistics Directorate). 96 children were enrolled in the study.

Plasma concentration of zinc (PCZ) were determined in all the patients. The colorimetric method with Br-PAPS final point (CV% 0.98% - 4.64%) was used for the zinc dosage. The readings were performed with the automatic analyzer Beckman Synchron CX5 (Beckman Coulter Inc, USA). Values ranging between 9.8-16.8 μmol/l were considered normal.

Measurement of naked body weight of the children was done with an electronic scale for infants and children with an accuracy of 10g (Momert Co, model no.6425, Hungary). The maximum weight measured with this scale was 20 kg. Height was measured in the morning, between 8 AM and 10 AM. For children under the age of 2, height was measured in the supine position using a rigid pediatric height rod (Fazzini, model no. S209, Italia), with a measuring range of 0-100cm, and an accuracy of 0.1cm. The height of children with ages above two years was measured in the standing position, using a stadiometer (Fazzinni, model no.S7700, Italia) with a measuring range between 85-200cm and an accuracy of 0.1cm.

Anthropometric indices were calculated with the WHO Anthro version 3.2.2 package. The reference population was the one provided by the WHO database. Z-scores have been considered low for values below -2SD (stunting: HAZ<-2SD, wasting: WHZ<-2SD, underweight: WAZ<-2DS), normal between -2 SD ÷ + 2 SD and high above 2SD.

The statistical analysis was performed with IBM SPSS statistics. The values obtained for different parameters were considered primary data for calculating the correlation coefficient. In order to obtain an independent indicator, not related to measurement units, the Bravais-Pearson correlation coefficient (r) was used. The correlation coefficient, r, has a meaningful interpretation only for cases in which $p<0.05$.

RESULTS

During the studied period, 98 children have been declared eligible. Two of them were excluded at the request of their parents. A number of 96 children eventually participated in the study. The sample group was relevant with a probability of 95%. The main characteristics of the 96 subjects of the study are shown in Table 1.

Table 1.

Main characteristic features of the study group

Variable parameter	Study group (N = 96)
Male gender, N (%)	53 (55.30)
Age (months), M (SD)	19.5 (10.48)
Rural background, N (%)	51 (53.20)
PCZ (µmol/l), M (SD)	15.33 (1.49)
PCZ (µmol/l), N (%)	
low	0 (0)
normal	77 (80.2)
high	19 (19.8)
Z-score, M (SD)	
WHZ	-0.09 (1.13)
WAZ	-0.06 (1.34)
HAZ	-0.02 (1.32)

Abbreviations: WHZ –weight-for-height z-score; WAZ – weight-for-age z-score; HAZ – height-for-age z-score; M – mean; DS –standard deviation; N – number of patients, PCZ-plasma concentration of zinc.

In our study we did not find a correlation between PCZ and WHZ values (r=0.19, p=0.063), (Fig.1).

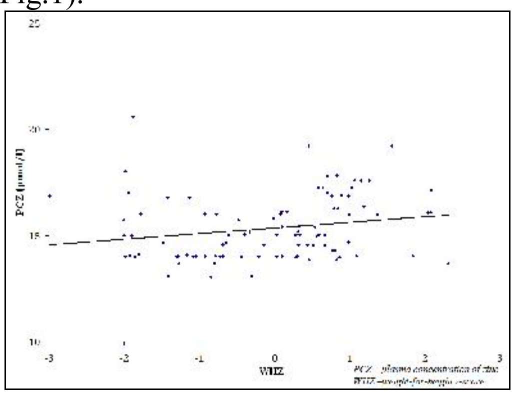

Fig. 1. Correlation between plasma zinc concentration and weight-for-height z-score

PCZ was moderately correlated with WAZ, (r=0.41, p<0.001), (Fig. 2), and respectively with HAZ (r=0.59, p<0.001), (Fig. 3).

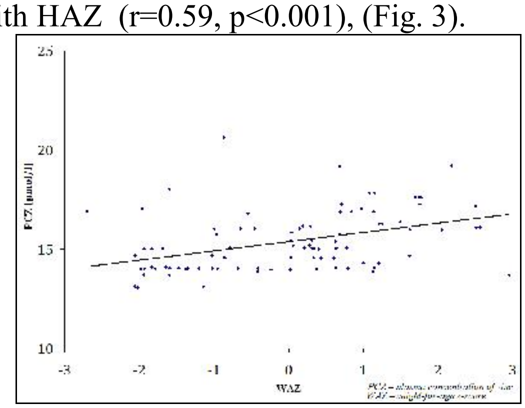

Fig. 2. Correlation between plasma zinc concentration and weight-for-age z-score

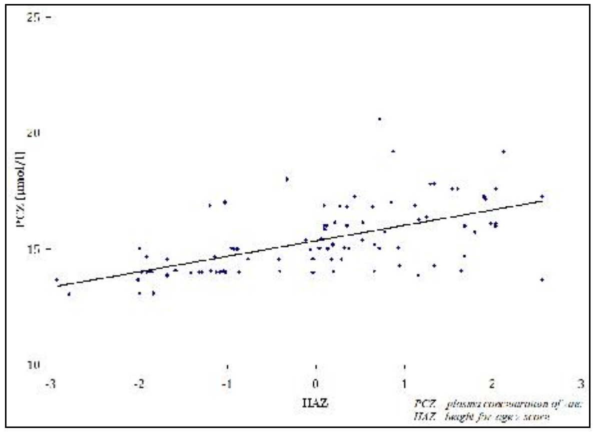

Fig. 3. Correlation between plasma concentration of zinc and height-for-age z-score

DISCUSSION

Zinc is one of the most important micronutrients. The lack of zinc deposits in the body means there is a continuous need for intake of zinc through alimentation. In the pediatric population, because of specific growth and development processes, there is an increased need of zinc intake.

In our study the plasma values of zinc were moderately correlated with WAZ. We obtained a positive correlation between the two observed variables. Gaining weight is influenced by alimentary habits and less often by the hormonal configuration. Different aliments have different contents of zinc. For instance, aliments from animal origin contain important quantities of zinc, protein and lipids. The energetic intake required by growing organisms is acquired in a proportion of 50-55% from carbohydrates, but the aliments containing carbohydrates usually have a poor zinc content (Graur, 2006). Nutritional deficiencies trigger a loss of weight, subsequent to the deprivation of young organisms of the nutrients required for a proper energy intake. Associated with these alimentary habits, an insufficient intake of zinc-rich aliments usually occurs. The scientific literature has so far been contradictory in regards to the correlation between WAZ and plasma zinc values. In 2013, Sezer RG and his collaborators have done a study on a group of 100 healthy children from Istanbul, all aged between 6-28 months. The authors of the study have reported a positive correlation between serum levels of zinc and body weight of the children in the study group (Sezer et al., 2013). A study conducted in 2010 by Beinner MA and collaborators on a group of Brazilian children aged between 6 and 24 months reported the lack of correlation between PCZ and anthropometric indices (Beinner et al., 2010).

In our study we obtained a positive correlation between PCZ and HAZ values for children in the observed group. The zinc ion is involved in stimulation of bone formation and mineralization (Yamaguchi, 1998; Yamaguchi, Inamoto, 1986). Linear growth of children is coordinated by the growth hormone and thyroid hormones. In 2000, a study conducted by MacDonald RS on a group of rats that were fed a low zinc diet recorded a decrease of the serum level of Insulin-like Growth Factor (IGF-I) and a halt in the growth of animals (MacDonald, 2000). The administration of IGF-I did not resume growth in the studied animals. The author suggests that zinc is involved in the cellular signaling pathways through which cell proliferation is accomplished in response to IGF-I. Duda KM and collaborators assert that, in the presence of the zinc ion, there is an increased chemical affinity of the growth hormone for the specific lactogenic receptor. To perform this, the microelement connects the hormonal amino-acid residues (H_{18}, E_{174}) with the adjacent residues of the receptor (D_{187}, H_{188}) (Duda, Brooks, 2003). Another process through which zinc promotes the growth of the human organism is the dimerization of the growth hormone, synthesized by the anterior pituitary gland (Kaji, 2006; Cunningham et al., 1991). In a study performed on a group of 24 children with growth hormone deficiency, Şıklar Z and collaborators recorded an accelerated rate of the linear growth after supplementation with zinc (Siklar et al., 2003). So far, the relation between zinc and the thyroid gland has not been studied in depth. Presently, it is known that thyroid hormones affect the absorption and excretion of zinc, while zinc deficiency disturbs thyroid functions (Ertek et al., 2010). In a study on a group of 201 Turkish subjects, Ertek S and collaborators showed a positive correlation between serum zinc level and the concentration of triiodothyronine in patients with normally functioning thyroid (Ertek et al., 2010). According to the same study, serum levels of zinc are negatively correlated with thyroid size in patients with nodular goiters and positively correlated with serum levels of specific autoantibodies (anti-thyroid peroxidase and anti-thyroglobulin) in patients with autoimmune thyroiditis (Ertek et al., 2010). Maxwell C and collaborators claim that zinc supplementation has a positive impact on triiodothyronine synthesis in zinc-depleted subjects (Maxwell, Volpe, 2007). Although zinc bears a role in cellular growth, and in the regulation of the most important hormones for the development of children, medical literature is still inconclusive concerning the relation zinc between zinc and HAZ. On one hand, Sezer RG directed a study on 100 healthy children from Istanbul, Turkey, with ages between 6 and 28 months, showing the lack of correlation between serum levels of zinc and the height of the subjects (Sezer et al., 2013). On the other hand, Wessels KR and collaborators have identified a positive correlation between zinc deficiency and a small-for-age height (Wessells, Brown, 2012). A study designed by Brown K RA and collaborators asserts that the rate of growth retardation is most closely correlated with nation-wide zinc deficiency (Brown et al., 2004). A meta-study conducted by Brown KH and collaborators, which reviewed 33 eligible trials performed on children under the age of 12, not suffering of severe protein-caloric malnutrition, concluded that zinc supplementation resulted in a significant increase in height for the observed subjects, with highest increase for children over 6 months with low height for age (Brown et al., 2002).

The statistic analysis conducted by us indicates a lack of correlation between plasma zinc levels and WHZ. Other results in scientific literature have been contradictory in regards to this relationship. A 2010 study conducted by Beinner MA and collaborators on a group of Brazilian children with ages between 6 and 24 months, claims the absence of any correlation between plasma zinc levels and anthropometric indices (Beinner et al., 2010). In a study by Chen XC and collaborators on a group of preschool Chinese children, a positive correlation between WHZ and PCZ has been observed (Chen et al., 1985).

Our study is the first of this kind in Romania, observing human subjects with ages between 0-3 years.

CONCLUSION

In children under the age of 3, plasma values of zinc are influenced by weight, height and not influenced by weight.

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