

Pediatric trace elements. Clinical updates

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RESUMEN

Durante la etapa temprana, los lactantes consumen una dieta predominantemente láctea. La leche es un producto natural, rico en oligoelementos (aproximadamente 1 g/100 mL). Los oligoelementos son compuestos inorgánicos que no se sintetizan en el cuerpo, donde existen en pequeñas cantidades; por lo tanto se deben obtener de los alimentos, ya que son esenciales para la vida. El presente artículo de revisión da a conocer los estudios más recientes de los oligoelementos y su fuente de obtención, así como la importancia de su uso en la nutrición parenteral total.

Palabras Clave: Oligoelementos, alimentos naturales, nutrición parenteral total, compuestos inorgánicos, lactantes.

ABSTRACT

During early life, infants usually consume a predominant milk diet. This is a natural food rich in trace elements (approximately 1 g/100 mL). Trace elements are not inorganic compounds synthesized in the body, which contains only small amounts; they can be obtained from natural food, since they are necessary for human life. This paper reviews the updated information on trace elements, their source from natural foods, and their importance in parenteral nutrition.

Key words: Trace elements, natural foods, total parenteral nutrition, inorganic compounds, infants.

During early life, infants usually consume a diet heavily dominated by milk. It is generally believed that breast-fed infants absorb adequate quantities of minerals and trace elements, whereas there is some concern on how well infants utilize these nutrients from cow's milk formula and other types of infant diets. Therefore, most infant formulas contain much higher concentrations of minerals and trace elements

than those in breast milk (Table 1). It is difficult to assess minerals and trace elements status in infants, as well as to ascertain the potential adverse consequences of either suboptimal or excessive intakes of calcium, magnesium, iron, zinc, copper, manganese, and selenium¹. It is equally hard to measure the bioavailability of protein fragmentation in the gastrointestinal tract and the chemical interactions of trace elements².

This study shows that milk is a natural food, rich in trace elements (approximately 1 g/100 mL) whose concentration varies due to genetic factors, type of feed consumed by the cattle and also resulting from contamination in the area of production. The average mineral content of milk in mg/L was: calcium 1179, magnesium 109.7, zinc 5.89, phosphorus 637.1, copper 0.15, cadmium < 0.01, chromium < 0.02, iron 0.59, lead < 0.04, manganese < 0.02, nickel 0.36³. Some natural foods also have trace elements, and they are inexpensive (Table 2).

Concentration of iron in cow's milk, 0.40-0.59 µg/mL, was found to be quite similar to that of human milk, 0.20-0.69 µg/mL. Copper concentration of cow's milk (0.06-0.09 µg/mL) is lower than in human milk (0.24-0.50 µg/mL) whereas zinc concentration is higher in cow's

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Table 1. The American of Pediatric Academy suggests the next values in infant formulas

<i>Substance</i>	<i>Minimum level</i>	<i>Máximum level</i>
Calcium (mg)	60	*
Fosphorus (mg)	30	*
Magnesium (mg)	6	*
Iron (mg)	0.15	2.5
Iodine (mg)	5	25
Zinc (mg)	0.5	*
Cuprum (µg)	60	*
Manganese (µg)	20	60
Potassium (mg)	80	200
Chloride (mg)	55	150
Selenium (µg)	3	*

*Insertan dates

milk (3.23-5.15 µg/mL) than in human milk (1.16-3.83 µg/mL). Cow's milk contains 4 to 5 times more calcium and magnesium, 854-1430 µg/mL and 87-131 µg/mL, respectively, than human milk (220-252 µg/mL and 26-35 µg/mL). Casein fraction in cow's milk contains a large proportion of the total amount of the elements cited above (Fe 24%, Cu 44%, Zn 84%, Ca 41%, Mg 25%) whereas human casein only binds minor amounts (Fe 9%, Cu 7%, Zn 8%, Ca 6%, Mg 6%). Whey proteins bind a major part of these elements in human milk, but not in cow's milk ⁴.

Trace elements are important substances for biochemical reactions in the body; likewise, these take part in hormone synthesis, food digestion, cell reproduction and the immune system ⁵. Trace elements are inorganic compounds which are not synthesized in the body; these are contained in minimum quantity, and they are necessary in food consumption, are most important for human life ⁶.

The current way of life and industrialization of food industry have caused many people deprivation of adequate amounts of trace elements. This results in the development of many chronic diseases ⁷. Recent studies have shown the latest findings on trace elements and their possible biological effects (Table 3); 20% of these studies have been made in Mexican population.

Moreover, inpatients have the option of receiving trace elements in total parenteral nutrition (TPN), which is a therapeutic tool if trace elements are below amounts required by the body ³⁹. TPN is a therapeutic and prophylactic life sustaining method for patients in high risk of malnutrition, and cannot be fed by mouth. It is an intravenous method to supply every element required to maintain or to recover an adequate nutritional state ⁴⁰.

In order to determine an individual's nutritional state, the physician should enquire about his nutritious regimens and health problems, carrying out a physical exam and running tests on blood nutrient values and of substances

Table 2. Usual doses of trace elements in foods consumed by infants and their natural source

<i>Name</i>	<i>Symbol</i>	<i>Doses per day</i>	<i>Natural source</i>
Iron	Fe	6-10 mg	Yeast, beans, wheat germ, chickpea, oats, beef liver, spinach.
Iodine	I	40-50 µg	Onion, seafood, seaweed
Zinc	Zn	5-10 mg	Milk, egg, meat, yeast
Magnesium	Mg	40-60 mg	Oats, almond, beans, wheat, lentils, coconut, rye, wheat germ
Selenium	Se	10-15 µg	Legumes, milk, meat, cereal, seafood
Cuprum	Cu	0.4 – 0.7 mg	Yeast, beef liver, oats, alfalfa, olives, avocado, barley.
Manganese	Mn	0.3 – 1 mg	Oats, avocado, alfalfa, beans, almond, nuts, coconut, spinach, peanuts, lettuce
Sulfur	S	NO	Peanuts, beef liver, oats, egg, lentils, parsley, nut, broccoli, fresh cod
Flúor	F	0.1 – 1 mg	seafood, fruits, meats and vegetables.
Cromium	Cr	0.01 – 0.06 mg	Chicken, milk, yeast
Cobalto	Co	No infants 1,2 µg	Milk, alfalfa, sardine
Phosphorus	P	300-500 mg	Yeast, yolk, sardine, soybean, almond, peanuts, oats, lentils
Molibdenum	Mo	15-40 µg	Milk, legumes, vegetables
Níquel	Ni	60 – 150 µg	Chocolate, nuts, cereal
Sodium	Na	115-750 mg	Salt, olives, margarine, milk serum, canned goods, wheat bread
Calcium	Ca	400-600 mg	Milk, soybean, molasses, watercress, parsley, beans, hazelnuts, lentils, salmon, cheese
Potassium	K	275-1200 mg	Milk, legumes, meat, yeast and fruit
Chloride	Cl	275-1200 mg	Milk, salt, molasses, coconut, olive

Table 3. Studies of trace elements in recent years (continúa en la siguiente página)

Symbol	Biological effects	Ref.
Zn	Zinc and micronutrients treatment increased the lymphocyte ratios of CD4(+) to CD8(+) and of CD4(+)CD45RA(+) to CD4(+)CD45RO(+).	8
Zn	Vitamin A plus zinc reduce <i>Giardia lamblia</i> incidence, whereas zinc supplementation increases <i>Ascaris lumbricoides</i> incidence but decreases <i>Entamoeba histolytica</i> -associated diarrhea.	9
Fe	Anemia was mostly associated with iron deficiency and with a lesser proportion of folate and vitamin A deficiencies. Vitamin A deficiency might be overestimated since iron deficiency may lower serum retinol concentrations.	10
Se	Concentrations of minerals and trace elements in formulas for full-term infants are generally higher than in human milk, and all appear to be more than adequate, with the possible exception of selenium, which may need to be increased in some formulas.	11
Zn	The incidence rate/ratio (IRR) of developing a cold (IRR 0.64; 95% CI 0.47 to 0.88) (P = 0.006), school absence (P = 0.0003) and prescription of antibiotics (P < 0.00001) was lower in the zinc supplementation.	12
Fe	Almost one-fourth of US children under 12 years of age, and 30% of 2-year-olds, use vitamins, fluoride, and iron supplements in a given week.	5
Se, Zn	High levels of serum lead and mercury and low levels of zinc and selenium induce some disturbances in the antioxidant system in children with recurrent wheezing.	13
Fe	Maternal hepcidin is not significantly altered as a function of placental infection and/or anemia.	14
Zn	Zinc reduces the frequency and improves recovery rates of any type of diarrhea and has better compliance and outcome with its use in suspension form.	15
Fe, Zn	Micronutrients powder probably enhances absorption of high native iron content of complementary foods in cereals and/or legumes.	16
Zn	Aspects of intellectual functioning including working memory, inhibitory control, and fine motor functioning among offspring were positively associated with prenatal iron/folic acid supplement in an area where iron deficiency is prevalent.	17
Zn	Zinc is safe in HIV-infected adults and children. It may have similar benefits in HIV-infected children and adults, and uninfected children with diarrhoea, as it does in HIV-uninfected children	18
Fe	<i>H. pylori</i> infection is associated with higher prevalence of anemia in school-age children regardless of socioeconomic variables.	19
Fe	One child was found to have a sagittal sinus venous thrombosis caused by severe dietary iron deficiency anemia.	20
Fe	Oral iron therapy, in appropriate doses and for sufficient duration, is an effective first-line strategy for most patients and in selected patients for whom intravenous (IV) iron therapy is indicated.	21
Fe	The regulatory effect of IL-6 in human hepcidin production suggests that iron deficiency is a causal link between IL-6 and anemia of chronic disease.	22
Zn	Zinc reduced the mean weight of body mass index significantly. Clinical application of zinc supplementation in childhood obesity should be carried out in future studies.	23
Se, Fe	Alterations in serum levels of trace elements in obese children may play a role in the pathogenesis of obesity.	24
Mn	Airborne Mn environmental exposure is inversely associated with intellectual function in young school-age children.	25
Se	Serum selenium level in children with simple febrile seizures was significantly lower than in the nonseizure control group. It seems that there is an association between serum selenium deficiency and simple febrile seizures.	26
Fe	Children 6-60 months of age with smear-positive malaria and anemia (hematocrit < 33%) should receive iron (2 mg/kg/day) plus folate (5 mg/day) or folate alone. Iron supplementation improved hematologic recovery in children with malarial anemia.	27
Zn	Profound changes in the thymus can also be seen in deficiency of vitamins and trace elements. Zn deficiency causes a substantial thymic atrophy.	28
Fe	Ferrous fumarate and ferrous sulfate are well absorbed in non-anemic, iron sufficient infants and young children, and can be recommended as a useful fortifying compound for complementary foods designed to prevent iron deficiency.	29
Se	Se status is depressed in pediatric patients with burns and the recommended intake for healthy children is insufficient for this population.	30
Zn	Zinc supplementation is effective in hepatic encephalopathy and consequently improves patient health-related quality of life.	31

Table 3. Studies of trace elements in recent years (continuación)

Symbol	Biological effects	Ref.
Zn	Concentrations of Zn, Ca, K, and Mg were lower in scalp hair and blood but higher in urine samples in children with night blindness.	32
I	Iodine intake of infants up to four months of age should be raised from currently 40 µg/d to at least 60 µg/d.	33
Fe	In children older over six years of age, there was a nearly 2-fold increase in iron absorption from ferrous fumarate given with orange juice	34
Mn	Brain MRI showed a high frequency (64%) of T1 hyperintensity in basal ganglia of patients with portal hypertension, which correlated positively with blood manganese levels.	35
Se	Studies on children exposed to methyl-mercury (MeHg) by ingestion Se-rich ocean fish showed improved their IQ instead of harm.	36
Fe	Lead level ≥ 10 µg/dl was significantly associated with anemia, decreased iron absorption and hematological parameters disturbances. High blood lead levels were associated with low serum iron and ferritin	37
Se	Cerebro-spinal fluid Se values were 32 times lower compared with those for plasma and there was an association between CSF Se and GPX activity.	38

Zn=Zinc, Fe=Iron, Se=Selenium, Mn=Manganese, I=Iodine.

related to these values: hemoglobin, thyroid hormone or transferrin, the latter as indicator of metabolic damage³.

To determine a person's nutritious regimen background, the physician should also ask what foods he ingested in the last 24 hours, and what foods he or she takes regularly. The patient can then make a list all of the foods taken for three days. A person's behavior, general aspect, body fat distribution and the body organ functioning can be assessed during the physical exam.

An individual's nutritional state can be determined in different ways. One of them is to measure size and weight, and compare them with standard tables. Another way is to determine the body mass index, i.e. by dividing weight (kg) by the square height (m²). If the body mass index is between 20 and 25, it is considered normal for males or females⁴¹.

It is very important to define the intended type of parenteral nutrition intravenously for an individual, once his nutritional state has been determined⁴².

The preparation of parenteral nutrition is more a complex formula due to the large number of components it requires: amino acids, carbohydrates, lipids, electrolytes, vitamins and trace elements. There is the risk of incompatibility among them, limited stability, and potential contamination which might adversely affect the pediatric patient, sometimes with serious consequences⁴³, given the fact that pediatric standardized formulas are still unavailable.

Trace elements are therapeutic tools necessary for human life and should be prescribed or recommended by the physician or the specialist in pediatric nutrition.

REFERENCES

- Lönerdal B. Effects of milk and milk components on calcium, magnesium, and trace element absorption during infancy. *Physiol Rev* 1997;77(3):643-69.
- Rolland-Cachera MF, Dhegheer M, Akrouf M et al. Influence of macronutrients on developments: a follow up study of nutrition and growth from 10 months to 8 years. *Int J Obes* 1995;19:573-8.
- Alanis Guzmán MG, Castro Góngora JE. Mineral composition of milk produced in Monterrey, N.L. México. *Arch Latinoam Nutr* 1992;42(4):456-9.
- Fransson GB, Lönerdal B. Distribution of trace elements and minerals in human and cow's milk. *Pediatr Res* 1983;17(11):912-5.
- Irlam JH, Visser MM, Rollins NN, Siegfried N. Micronutrient supplementation in children and adults with HIV infection. *Cochrane Database Syst Rev* 2010;8(12):CD003650.
- Food and nutrition aboard, National Research Council. Recommended Dietary Allowances. 10th ed. Washington D.C.: National Academy Press; 1989.
- Henche Morilla AL, Romero Montero C, Llorente González C. Levels of oligo-elements and trace elements in patients at the time of admission in intensive care units. *Nutr Hosp* 1990;5:338-44.
- Sandstead HH, Prasad AS, Penland JG, Beck FW, Kaplan J, Egger NG, Alcock NW, Carroll RM, Ramanujam VM, Dayal HH, Rocco CD, Plotkin RA, Zavaleta AN. Zinc deficiency in Mexican American children: influence of zinc and other micronutrients on T cells, cytokines, and antiinflammatory plasma proteins. *Am J Clin Nutr* 2008;88(4):1067-73.
- Long KZ, Rosado JL, Montoya Y, de Lourdes Solano M, Hertzmark E, DuPont HL, Santos JI. Effect of vitamin A and zinc supplementation on gastrointestinal parasitic infections among Mexican children. *Pediatrics* 2007;120(4):e846-55.
- Villalpando S, Pérez-Expósito AB, Shamah-Levy T, Rivera JA. Distribution of anemia associated with micronutrient defi-

- ciencias other than iron in a probabilistic sample of Mexican children. *Ann Nutr Metab* 2006;50(6):506-11.
11. Flynn A. Minerals and trace elements in milk. *Adv Food Nutr Res* 1992;36:209-52.
 12. Singh M, Das RR. Zinc for the common cold. *Cochrane Database Syst Rev* 2011;16(2):CD001364.
 13. Vernacchio L, Kelly JP, Kaufman DW, Mitchell AA. Vitamin, fluoride, and iron use among US children younger than 12 years of age: results from the Slone Survey 1998-2007. *J Am Diet Assoc* 2011;111(2):285-9.
 14. Razi CH, Akin O, Harmanci K, Akin B, Renda R. Serum heavy metal and antioxidant element levels of children with recurrent wheezing. *Allergol Immunopathol (Madr)* 2011 Jan 12. [Epub ahead of print].
 15. Van Santen S, de Mast Q, Luty AJ, Wiegerinck ET, Van der Ven AJ, Swinkels DW. Iron homeostasis in mother and child during placental malaria infection. *Am J Trop Med Hyg* 2011;84(1):148-51.
 16. Habib MA, Soofi SB, Bhutta ZA. Effect of zinc in tablet and suspension formulations in the treatment of acute diarrhoea among young children in an emergency setting of earthquake affected region of Pakistan. *J Coll Physicians Surg Pak* 2010;20(12):837-8.
 17. Troesch B, van Stuijvenberg ME, Smuts CM, Kruger HS, Biebinger R, Hurrell RF, Baumgartner J, Zimmermann MB. A micronutrient powder with low doses of highly absorbable iron and zinc reduces iron and zinc deficiency and improves weight-for-age Z-scores in South African children. *J Nutr* 2011;141(2):237-42.
 18. Christian P, Murray-Kolb LE, Khatry SK, Katz J, Schaefer BA, Cole PM, Leclercq SC, Tielsch JM. Prenatal micronutrient supplementation and intellectual and motor function in early school-aged children in Nepal. *JAMA* 2010;304(24):2716-23.
 19. Muhsen K, Barak M, Henig C, Alpert G, Ornoy A, Cohen D. Is the association between *Helicobacter pylori* infection and anemia age dependent? *Helicobacter* 2010;15(5):467-72.
 20. Habis A, Hobson WL, Greenberg R. Cerebral sinovenous thrombosis in a toddler with iron deficiency anemia. *Pediatr Emerg Care* 2010;26(11):848-51.
 21. Pasricha SR, Flecknoe-Brown SC, Allen KJ, Gibson PR, McMahon LP, Olynyk JK, Roger SD, Savoia HF, Tampi R, Thomson AR, Wood EM, Robinson KL. Diagnosis and management of iron deficiency anaemia: a clinical update. *Med J Aust* 2010;193(9):525-32.
 22. Arlet JB, Hermine O, Darnige L, Ostland V, Westerman M, Badoual C, Pouchot J, Capron L. Iron-deficiency anemia in Castleman disease: implication of the interleukin 6/hepcidin pathway. *Pediatrics* 2010;126(6):e1608-12.
 23. Kelishadi R, Hashemipour M, Adeli K, Tavakoli N, Movahedian-Attar A, Shapouri J, Poursafa P, Rouzbahani A. Effect of zinc supplementation on markers of insulin resistance, oxidative stress, and inflammation among prepubescent children with metabolic syndrome. *Metab Syndr Relat Disord* 2010;8(6):505-10.
 24. Tascilar ME, Ozgen IT, Abaci A, Serdar M, Aykut O. Trace elements in obese Turkish Children. *Biol Trace Elem Res* 2010; [Epub ahead of print].
 25. Riojas-Rodríguez H, Solís-Vivanco R, Schilman A, Montes S, Rodríguez S, Ríos C, Rodríguez-Agudelo Y. Intellectual function in Mexican children living in a mining area and environmentally exposed to manganese. *Environ Health Perspect* 2010;118(10):1465-70.
 26. Mahyar A, Ayazi P, Fallahi M, Javadi A. Correlation between serum selenium level and febrile seizures. *Pediatr Neurol* 2010;43(5):331-4.
 27. Gara SN, Madaki AJ, Thacher TD. A comparison of iron and folate with folate alone in hematologic recovery of children treated for acute malaria. *Am J Trop Med Hyg* 2010;83(4):843-7.
 28. Savino W, Dardenne M. Nutritional imbalances and infections affect the thymus: consequences on T-cell-mediated immune responses. *Proc Nutr Soc* 2010;69(4):636-43.
 29. Harrington M, Hotz C, Zeder C, Polvo GO, Villalpando S, Zimmermann MB, Walczyk T, Rivera JA, Hurrell RF. A comparison of the bioavailability of ferrous fumarate and ferrous sulfate in non-anemic Mexican women and children consuming a sweetened maize and milk drink. *Eur J Clin Nutr* 2011;65(1):20-5.
 30. Dylewski ML, Bender JC, Smith AM, Prelack K, Lydon M, Weber JM, Sheridan RL. The selenium status of pediatric patients with burn injuries. *J Trauma* 2010;69(3):584-88.
 31. Takuma Y, Nouse K, Makino Y, Hayashi H, Takahashi H. Clinical trial: oral zinc in hepatic encephalopathy. *Aliment Pharmacol Ther* 2010;32(9):1080-90.
 32. Afridi HI, Kazi TG, Kazi N, Kandhro GA, Baig JA, Shah AQ, Wadhwa SK, Khan S, Kolachi NF, Shah F, Jamali MK, Arain MB, Sirajuddin A. Evaluation of Essential Trace and Toxic Elements in Biological Samples of Normal and Night Blindness Children of Age Groups 3-7 and 8-12 Years. *Biol Trace Elem Res* 2010 Sep 4. [Epub ahead of print].
 33. Remer T, Johnner SA, Gärtner R, Thamm M, Kriener E. Iodine deficiency in infancy - a risk for cognitive development. *Dtsch Med Wochenschr* 2010;135(31-32):1551-6.
 34. Balay KS, Hawthorne KM, Hicks PD, Griffin IJ, Chen Z, Westerman M, Abrams SA. Orange but not apple juice enhances ferrous fumarate absorption in small children. *J Pediatr Gastroenterol Nutr* 2010;50(5):545-50.
 35. Pinto RB, Fröhlich PE, Pitrez EH, Bragatti JA, Becker J, Cornely AF, Schneider AC, da Silveira TR. MR findings of the brain in children and adolescents with portal hypertension and the relationship with blood manganese levels. *Neuropediatrics* 2010;41(1):12-7.
 36. Ralston NV, Raymond LJ. Dietary selenium's protective effects against methylmercury toxicity. *Toxicology* 2010;278(1):112-23.
 37. Hegazy AA, Zaher MM, Abd El-Hafez MA, Morsy AA, Saleh RA. Relation between anemia and blood levels of lead, copper, zinc and iron among children. *BMC Res Notes* 2010;12(3):133.
 38. Tondo M, Moreno J, Casado M, Brandi N, Sierra C, Vilaseca MA, Ormazabal A, Artuch R. Selenium concentration in cerebrospinal fluid samples from a pediatric population. *Neurochem Res* 2010;35(8):1290-3.
 39. Calderón GD, Hernández GE, Barragán MG, Guillé PA, Juárez OH. Parenteral nutrition given to children and adults: Experience of a procedure applied in Mexico. *Proc West Pharmacol Soc* 2008;51:35-7.
 40. Jaramillo RO. Nutrición parenteral total (NPT). Curso sobre soporte nutricional. Canizales. Colombia. 1982.
 41. Merck Sharp & Dohme de España, S.A. Madrid, España; 2005.
 42. Esarte Muniáin JM, Escartín Valderrama J, Miguel Ardevines C, Dobón Rascón MA, Cebollero Benito MP, Valenzuela Martínez MJ, Ibáñez Mirallas JP, Vázquez Sancho M. Nutrición parenteral periférica: una alternativa para el soporte nutricional en cirugía. *Cir Esp* 2000;67:381-7.
 43. Inaraja MT, Castro I, Martínez MJ. Formas farmacéuticas estériles: mezclas intravenosas, citostáticos, nutrición parenteral. *Farmacia Hospitalaria* 1995;487-506.