



THE SUPPLEMENT

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ZINC AND CYSTIC FIBROSIS

Prior to the 1960s little was known about zinc in human nutrition. Following Prasad's [1] identification of zinc deficiency in growth delayed men, zinc research expanded. By 1998 there had been such an increase in knowledge regarding the extent, causes, and effects of zinc deficiency, the NIH, with the Office of Dietary Supplements, convened a zinc conference to review available knowledge. [2] You are encouraged to review the proceedings of the NIH conference and/or the zinc chapter of a current nutritional biochemistry textbook.

Zinc metabolism is complex, fascinating, and not fully understood. Zinc, a micromineral, is involved in over 300 [3] enzymes. Therefore zinc deficiency presents both overtly and subtly. The underlying biochemical mechanism for most of the signs and symptoms remain unknown. Zinc was first introduced into the RDAs in 1974; the current DRI publication contains an excellent summary of zinc. [www.nap.edu]

Zinc homeostasis is sensitive and maintained through the intestinal absorption of both exogenous zinc and endogenous zinc. Food and zinc supplements are sources of exogenous zinc. Endogenous zinc is "recycled" zinc, in that it is excreted from the pancreas into the intestine and reabsorbed. A pancreatic ligand may also be necessary for zinc absorption. Absorption can be inhibited by: 1.) The presence of phytate and fiber; 2.) Undigested fat and protein; and 3.) Large amounts of other minerals, such as calcium and iron.

The addition of CF to the equation makes the topic even more intriguing. Zinc's role in numerous body functions, including appetite, growth, and immunity, plus its potential to be malabsorbed with fat and protein makes it of great interest in the care of persons who have CF. Chronic inflammation and use of steroids affect zinc status. A characteristic rash of severe zinc deficiency, as seen in the heritable condition of acrodermatitis enteropathica, has been the presenting symptom in some infants diagnosed with CF. [4] Zinc's importance for persons who have

CF is acknowledged in the most recent CFF Nutrition Consensus Statement. [5]

FEATURED PAPERS:

The scientific literature was searched for zinc and CF from the past five years. Three papers are reviewed.

Easley D. Krebs N. Jefferson M. Miller L. Erskine J. Accurso F. and Hambidge KM. Effect of pancreatic enzymes on zinc absorption in cystic fibrosis. J of Ped Gastro & Nutr. 26(2):136-9, 1998. Objective: To evaluate the effect of SPE replacement on zinc absorption in CF children and adolescents. **Subjects:** 4 boys, 4 girls; ages 7-17 yrs; all PI. **Methods:** Stable isotopes were given orally with meals. Meals were identical for the first 2 study days to control for exogenous zinc. SPE were withheld on day 1 or 2, after which they remained constant at the subject's usual dose. SPE were given with all meals and snacks. All stools were collected for 10 days and analyzed for total zinc and isotopic zinc. **Results:** Fractional absorption (zinc consumed minus zinc excreted) when receiving enzymes: 0.50 ± 0.29 vs. 0.38 ± 0.24 while not taking enzymes ($p=0.05$). **Conclusions:** Dietary zinc absorption is impaired by PI and improved with SPE.

SPECIAL POINTS OF INTEREST:

- *Zinc homeostasis is sensitive and maintained through the intestinal absorption of both exogenous zinc and endogenous zinc.*
- *Zinc's role in numerous body functions, including appetite, growth, and immunity, plus its potential to be malabsorbed with fat and protein makes it of great interest in the care of persons who have CF.*

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FEATURED PAPERS (cont.):

Krebs NF. Sontag M. Accurso FJ. Hambidge KM. Low plasma zinc concentrations in young infants with cystic fibrosis. J of Peds. 133(6):761-4, 1998.

Objective: To study the zinc status of infants with CF before and after the initiation of SPE. **Subjects:** 70 infants identified through newborn screening.

Methods: Cross-sectional, semi-longitudinal study of plasma zinc levels of infants based on SPE use.

Results: Infants not receiving SPE had mean plasma zinc concentration (10.4 ± 2.2 micro mol/L) that was significantly lower than infants receiving SPE for ≥ 2 weeks (11.8 ± 2.3 micro mol/L) ($P = .03$). 29% of infants not receiving SPE had levels in the deficient range. Data available on 30 infants prior to and following SPE use showed a significant increase of 1.64 ± 3.0 . **Conclusions:** Many infants were deficient at diagnosis and zinc should be considered among the micronutrients in the management of CF, especially infants.

Krebs NF. Westcott JE. Arnold TD. Kluger BM. Accurso FJ. Miller LV. Hambidge KM.

Abnormalities in zinc homeostasis in young infants with cystic fibrosis. Ped Res. 48(2): 256-61, 2000. Objective:

To evaluate the fractional absorption and fecal excretion of endogenous zinc based on type of feeding (human milk or infant formula) and level of fat malabsorption. **Subjects:** 15 infants (9 male) diagnosed through newborn screening. Mean age 1.8 ± 0.7 months. 7 were fed human milk. **Methods:** Cross-sectional design. Oral

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(KREBS, ET AL, 1998)**

and intravenous administration of zinc stable isotopes combined with traditional metabolic studies to measure dietary zinc intake, fractional absorption of exogenous dietary zinc, and fecal excretion of endogenous zinc. **Results:** Infants fed human milk showed significantly higher fractional absorption (0.40 ± 0.21) when compared to formula-fed infants (0.13 ± 0.06) ($p = 0.01$). Formula-fed infants had significantly higher dietary zinc intake and significantly higher total absorbed zinc ($p = 0.01$). Available data indicated twofold greater excretion of endogenous zinc for the formula-fed infants ($p < 0.05$); net absorption was negative for both feeding groups. There was positive correlation between endogenous fecal zinc losses and fecal fat excretion ($n = 9$, $r = 0.89$, $p = 0.001$). **Conclusions:** Fat malabsorption may interfere with normal conservation of endogenous zinc. Findings indicate impaired zinc homeostasis and may provide an explanation for sub optimal zinc status in young infants with CF prior to diagnosis and treatment.

DISCUSSION

This issue of The Supplement summarizes recent research contributing to a better understanding of zinc and CF. The 1998 Krebs, et al paper describes zinc deficiency in infants identified through newborn screening. This work, and the work of others, [6,7] supports the importance of prompt diagnosis of CF and identification of pancreatic status [5] so that appropriate SPE, macronutrient and micronutrient

supplementation, including zinc, can be initiated to promote optimal nutritional status.

The work of Easley, et al further supports the importance of SPE in relationship to zinc absorption. Zinc malabsorption was directly correlated with fat and protein malabsorption. As with other nutrients, [8] even when receiving SPE, the subjects showed wide interindividual variability in fractional zinc absorption.

Krebs' et al 2000 research showed that endogenous fecal zinc losses correlated with fat malabsorption. PS infants tended to have normal fractional absorption. However, positive net zinc absorption was never achieved by either breastfed or formula fed PI infants.

This result suggested impaired zinc homeostasis perhaps by interference with normal conservation of endogenous zinc and an inability to compensate with increased fractional absorption.

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CLINICAL APPLICATIONS

Optimal zinc nutrition is vital during periods of rapid growth. Food sources of zinc include high protein foods such as meats and cheeses. Whole grains contain more zinc than refined. Some breakfast cereals are fortified with zinc. Zinc supplements are available in many chemical forms. Factors including: solubility, bioavailability, taste, side effects, cost, dosing and intragastric pH impact effectiveness. [9] The best form for the person who has CF is unknown.

Zinc is necessary for hepatic synthesis of retinol-binding protein and mobilization of retinol from the liver; therefore, consider zinc supplementation when low vitamin A levels or night blindness do not respond to vitamin A supplementation. [10]

Although some work has been done to identify a more sensitive marker of zinc status, [11] plasma zinc concentration remains the current laboratory test used, even though the prevalence of zinc abnormalities may be underestimated. A normal value does not necessarily indicate normal status. As with some other lab tests, such as H/H (iron) and PT (vitamin K), plasma zinc may only identify those patients with moderate to severe deficiency. Those with mild deficiency may fail to be identified. Both overt symptoms of zinc deficiency (changes in appetite and growth) and more subtle symptoms (decreased immunity) can occur while plasma levels are well within normal reference ranges. Brown [12], using

findings of a meta-analysis of zinc supplementation trials with malnourished children, suggests that the change in serum zinc concentration can be used as a practical indicator to assess adherence to and absorption of the zinc supplement.

When zinc deficiency is suspected how does the CF Center RD proceed? First, the RD calculates the patient's usual zinc intake from: diet, vitamin and mineral supplements, and other sources such as oral supplements, and enteral/parenteral tube feedings. Usual SPE use is assessed. Inadequate zinc nutritional status may be resolved by use of appropriate SPE, diet, and supplemental multivitamin with zinc. The zinc content of the multivitamin must be confirmed since many liquid vitamins for nonCF infants and some chewable multivitamins do not contain zinc. If the patient has optimized both zinc intake and SPE use and zinc deficiency is still suspected, treatment with a six-month trial of zinc supplementation may be necessary. The recommended zinc supplement dose for nonCF children is about 1 mg elemental zinc/kg/day up to 10 to 15 mg/day. [Krebs, 2000]. Exact dosage amounts for children and adults who have CF remain unknown. As with other nutrients, people who have CF must be evaluated individually. The total daily zinc dose may need to be higher than that recommended for people who do not have CF to correct zinc insufficiency and to achieve optimal zinc status.

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