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Reviews

Dietary Zinc – Heavy Metal Interactions

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Abstract

Experimental evidence has indicated that dietary zinc level may modulate the accumulation and toxic response to lead, cadmium and mercury.

Insufficient zinc intakes have been shown to increase the risk associated with the exposure of animals to these heavy metals. On the other hand, moderate zinc supplements have been found to have a marked effect in preventing the deleterious effect produced by lead, mercury and cadmium.

The mechanism by which dietary zinc may influence risks from lead, cadmium and mercury is not fully understood; however, the factors involved in the absorption from the gastrointestinal tract are of considerable concern.

Keywords: toxic effects; heavy metal; industraial emissions.

Introduction

Zinc is classified as a Group II B post-transition member of the periodic table along with mercury and cadmium, non-essential metals of great toxicity. This element, unlike other transition metals, is relatively stable in its divalent state and does not undergo redox changes.

The essentiality of zinc for mammals was established in the 1930s. Studies reported by Vallee [35] show that zinc is a constituent of a number of metalloenzymes. More recent evidence has indicated that zinc is involved in numerous biological actions. Zinc was found to play a substantial role in both DNA and RNA production [37]. Furthermore, Endre et al. [6] and Chevalier et al. [4] have indicated that zinc is essential to maintaining integrity of the immune system. Genotoxic and epidemiologic studies indicate that zinc is essential for optimum resistance to cancer. Moreover, zinc is involved in the proper functioning of the cardiovascular, nervous, endocrine and respiratory systems [3, 32, 37].

Zinc in Soil and Zinc Uptake in Plants

Zinc in soil is in the form of soluble compounds and is easily taken up by plants. A mean concentration of soil zinc ranges from 30 ppm to 125 ppm; in Poland, the mean soil concentration of zinc is about 40 ppm . The majority of soil contains zinc in sufficient concentrations for plants, although areas of zinc-deficient soil have been revealed in various parts of the world. However, soil zinc levels may increase substantially as a result of anthropogenic activity. A high zinc level (above 1000 ppm) is toxic for several microorganisms [18].

The availability of soil zinc to plants depends on zinc concentration, plant species, and zinc forms; contamination of soil by zinc may increase its accumulation in the food chain. In Poland, a mean concentration of zinc in plants ranges from 10 ppm to 70 ppm. Palilionaceous plants, grain crops, and grass contain 24 ppm to 99 ppm, 26 ppm to 80 ppm, and 15 ppm to 79 ppm of zinc, respectively [31]. Vegetables contain higher amounts of zinc than fruit.

Zinc in Animal Tissues and Diets

Zinc content of animal tissues is 10 ppm to 200 ppm. Reports by Żmudzki et al. [39, 40] indicate that meat, kidneys, and liver contained about 35 ppm, 19 ppm, and 38 ppm of zinc, respectively. Zinc status of man and animals generally resembles zinc content in the diet and the physiological conditions of the individual. However, the zinc content of food products is altered by cooking and zinc bioavailability depends on several components of the diet. Current data from the US suggest that meat provides nearly 50% of zinc in the average diet, dietary products provide about 20%, and cereals and legumines provide the remainder [37]. Phytate, present in grain and vegetable components of the diet, was shown to inhibit zinc absorption. Other dietary inhibitors of zinc absorption include lignin, certain hemicelluloses, and calcium.

During the past 30 years, deficiency of zinc in man resulting from nutritional factors has been documented throughout the world. The prevalence of zinc deficiency is

high in populations that consume diets rich in phytate and dietary fiber, and little red meat [37].

Zinc Toxicity

Zinc is generally considered to be a relatively non-toxic metal and its increased intake is associated with decreased absorption from the gastrointestinal tract and enhanced excretion. Excessive accumulation of zinc in the body does not produce genetic abnormalities, unlike metals such as copper (Wilson's Disease) and iron (hemochromatosis). A 100-fold excess of zinc in a diet fails to create significant pathology. In humans, death was reported after the ingestion of about 45 g of zinc sulphate. However, this dose may be considered very massive in view of the fact that the daily requirement of zinc for man is 15 to 30 mg per day. Patients with sickle cell disease have been administered 600 mg of zinc sulphate for 1 year without any adverse effect [29], although extremely high zinc intake is reported to cause a variety of abnormalities in several organs and systems.

Possible Mechanisms of the Interaction of Zinc and Other Elements in the Gastrointestinal Tract

Zinc – heavy metal interactions can occur anywhere in the food chain. Significant interactions take place in the gastrointestinal tract. A completely satisfactory explanation for the interaction at the site of absorption is not available, although a few mechanisms have been proposed [7]:

1. Competition for uptake – several chemically-similar elements may share a common pathway for absorption, thus co-ingestion of two or more elements will result in competition for uptake into the mucosal cells. This mechanism has been proposed for zinc-iron interaction [15].
2. Competition for mineral binding ligands – several dietary constituents were identified as binding minerals and some of these can affect absorption from the lumen. When there is an excess of minerals only a limited quantity of each mineral can be bound. For example, less iron will be bound to phytate in the presence of high concentrations of zinc and hence more should be available for absorption [19].
3. Co-adaptation – the dietary intake of one mineral may produce intracellular transfer or mucosal trapping mechanism which then influence the absorption of another mineral. Thus, deficiency or sufficiency of one mineral can determine the absorptive efficiency of another. For example, essential metal deficiency/supplements may increase/decrease heavy metal absorption from the gastrointestinal tract [5].

Dietary Zinc – Heavy Metal Interactions

Lead

Lead occurs in all components of the earth's biosphere. Exposure to lead is an important health problem in many countries. Sources of exposure include the use of lead-glazed pottery for cooking and storing food, residing in areas with heavy traffic, canned food and the presence of lead in indoor and outdoor dust [30]. An estimated 85% of the total amount of lead introduced into the biosphere is attributed to the combustion of leaded gasoline. The major sources of lead are food, water, and dust, which account for more than 98% of unavoidable lead intake (about 50 μg/day). The estimated daily intake of lead from food for adult people is about 380 μg.

In Poland, the respective values for adults and children are 50 μg to 520 μg and 40 μg to 350 μg [18].

Ingested lead is poorly absorbed (5% to 15%) because of the low solubility of lead salts. However, the rate of absorption in children is about 25% to 50%, which is attributed to the composition of the diet. None of the sources in itself (with the exception of the air around smelting and battery plants), is enough to cause acute toxicity of lead, but all are likely to be involved in cases in which evidence of increased lead burdens is found [24].

The interaction of zinc and lead was determined about 25 years ago. Willouhghby et al. [38] found that when high doses of zinc were fed concomitantly with lead, signs of lead poisoning did not appear and tissue concentrations of lead in several organs of cows were not enhanced. More recently, Mahaffey and Michelson [23] have reported a similar pattern among other species with increased levels of zinc in the diet causing a decline in tissue lead accumulation and a reduction in associated physical signs of this metal poisoning.

Cerklewski and Forbes [2] have reported that increasing dietary zinc from 8 to 200 ppm in rats fed 50 or 200 ppm of lead produced a decrease in lead concentrations in tissues and urinary excretion of gamma-aminolevulinic acid, and inhibition of gamma-aminolevulinic acid dehydratase activity in the kidneys. The authors hypothesised that zinc and lead competed for similar binding sites on a metallothionein-like protein responsible for metal transport in the intestine because zinc did not affect urinary lead excretion and injected zinc had no effect on lead toxicity.

An inverse relationship between dietary zinc levels and lead toxicity was also reported by Flora et al. [8]. Albino rats administered lead and zinc orally for 21 days at a daily dose of 10 mg Pb/kg b.w. and 2 mg Zn/kg b.w. contained lower levels of hepatic and renal lead in comparison to rats on lead alone, and significantly ameliorated the lead induced inhibition of blood gamma-ALAD activity. However, zinc failed to restore the decreased level of Hb. A more recent study by Flora et al. [17] indicated that modification of the toxic effect of lead by zinc was much more pronounced when supplemental methionine was also involved.

Interaction of lead with zinc is also highly relevant to heme biosynthesis, which is impaired as a result of ALAD - a zinc - dependent enzyme inhibition by lead. According to Goering and Fowler [12] the lead inhibition of ALAD can be overcome by donating zinc to this zinc-requiring enzyme and chelation of lead.

Schmitt et al. [32] stressed that pre-school children from low-income families have been found to have deficiencies in dietary zinc and many premature infants may suffer from zinc depletion without showing any clinical signs of zinc deficiencies. Consequently, the children may be above-average risk of lead poisoning. The authors suggest that zinc supplements may be an effective way to prevent damage to children resulting from lead in the environment.

Cadmium

Cadmium is a relatively new metal discovered in 1818. Production of cadmium began in Upper Silesia, Poland.

Cadmium is a nutritionally non-essential metal and is present in varying concentrations in air, soil, water, and food. Smelters are a principal source of environmental cadmium contamination. However, municipal incineration of waste materials, the burning of fossil fuels, the use of phosphate fertilisers and the disposal of sewage sludge are also substantial emission sources [22, 24].

For the general population, dietary exposure is due to contamination of food and inhalation exposure is due to smoking; ambient air levels are generally low but may be elevated in occupational settings or in the immediate vicinity of smelters.

Estimated average daily intake of cadmium is about 60 μg in Great Britain, 23 μg to 120 μg in Poland, and 150 μg on the world scale [18]. However, daily intake up to 400 μg may occur in heavily polluted areas. Foods of animal origin usually contain greater concentrations; however, food of plant origin (especially cereal grains) may contribute large amounts of cadmium [11].

Parzyk et al. [26] reported that pregnant rats maintained on a diet containing zinc reduced to about 1/20 the level in a standard diet and intoxicated with cadmium given at a dose of 1.5 mg/kg b.w. on day 8 and 12 of gestation increased substantially the resorption rate and the percentage of malformed litters. The authors suggested that the effect resulted from zinc deficiency. Experiments with young Japanese quail revealed that birds fed a diet containing 62 ppb cadmium and about half the normal dietary zinc intake increased cadmium contents in the liver [10].

The role of continuous dietary zinc deficiency on the metabolism of cadmium was studied by Waalkes [36]. Rats fed a diet with a decreased zinc level from 60 ppm (standard diet) to 7 ppm for 9 weeks were also maintained on a cadmium supplemented diet from 12.5 to 200 ppm. The zinc deficient diet markedly increased cadmium content in the liver, kidneys and testes.

Low zinc levels (5 ppm) in a diet produced an enhanced renal cadmium level after chronic oral exposure of rats to 0.5 or 10 ppm cadmium in drinking water [25].

On the other hand, Jacobs et al. [16] examined single supplements of zinc, copper, or manganese in one-day-old Japanese quail fed a basal diet enriched with 145 μg Cd/kg. When the supplemented diets were fed for 7 d only zinc had a protective effect against cadmium. Zinc reduced cadmium in the jejunum-ileum, liver and kidney by about 66%, 21%, and 11%, respectively. Moreover, feeding the experimental diets for 2 weeks resulted in similar responses. Supplements of zinc in excess of the young turkey's requirement declined the hock and feather abnormalities produced by 80 ppm dietary cadmium [35]. Supplemental zinc (75 ppm) produced an increase in the hematocryt of severely anemic Japanese quail fed 75 ppm cadmium [9]. Similar beneficial effects were reported for dietary doubling supplements of zinc (60 ppm) in Japanese quail fed 0.145 ppm cadmium [17].

Kulikowa-Karpińska et al. [21] used two levels of cadmium sulphate (5 mg/dm^3 and 50 mg/dm^3) and one level of zinc sulphate (250 mg/dm^3) in tap water given to rats to determine the effect of zinc on cadmium accumulation in rat organs. When rats drank the water with the highest level of cadmium along with zinc, hepatic and renal cadmium concentrations decreased by about 50% and 70%, respectively. In contrast, rats drinking tap water fortified with zinc after a 2-week cadmium exposure decreased cadmium levels only in the serum. When the cadmium level in tap water was lowered to 5 mg/dm^3, zinc significantly decreased serum, splenic, renal and bone cadmium. However, hepatic cadmium was enhanced two-fold.

In contrast, Groten et al. [14] failed to show any decrease in whole-body contents of cadmium in rats fed for 8 weeks a diet containing 30 mg Cd/kg and an 8-fold increased zinc level in comparison to a standard diet. However, the authors demonstrated a significant reduction in cadmium levels in kidneys and liver along with a reduction of cadmium toxicity in rats fed a diet enriched with calcium/phosphorus, iron and zinc.

Mercury

Mercury occurs in the environment largely as a result of vaporization or degassing of the earth's crust, mainly through volcanic gases and ocean evaporation. Anthropogenic sources contribute 10% to 80% of atmospheric mercury, including combustion of fossil fuels, metal smelting, chlorine production, and pollution of water by mine tailing drainage.

Food, especially fish, is the most important source of mercury exposure for the general public. Average dietary intake of mercury ranges from 2 μg to 7 μg. However, in Poland the results presented by Sprengier-Juszkiewicz [34] indicate that the daily intake of mercury is about 6 μg, 15 μg, and 14 μg for children, teenagers, and adults, respectively. Gastrointestinal absorption of mercury is about 15% and 95% for inorganic and methylmercury forms, respectively.

Relatively little attention has been paid to the effect of zinc on mercury content and toxicity in the body. Kulkova et al. [20] report an effect of diets marginally deficient in zinc (6, 8 or 40 ppm) and contaminated with 10 ppm inorganic mercury on mercury content in selected tissues. A 4-week feeding the deficient diets markedly enhanced mercury accumulation in rat kidneys and liver. Moreover, the organ concentrations of mercury revealed an inverse relationship with zinc content in the diets. The authors stressed that a marginal zinc deficiency may have a serious consequence for the toxic effect of small doses of mercury.

The effects of a 4-week feeding with a diet containing 10 times (450 ppm) the zinc level of a standard diet on inorganic mercury kinetics in the carcass and organs was studied in rats by Grosicki and Kowalski [13]. AUC values revealed a 37% decline in mercury contents in the carcass of rats. Additionally, substantial decreases in organ mercury, especially in the kidneys, liver and muscles, were found in rats fed the zinc-enriched diet. The antagonistic effect of zinc on mercury was thought to result from its interference in mercury absorption from the alimentary tract. Moreover, alterations in the elimination curve of radiomercury after intraperitoneal injection suggested a zinc-mercury interaction outside the digestive tract.

Conclusions

The available data indicate that food is a marked source of lead, cadmium and mercury. Moreover, heavy metal intakes from other sources also occur, especially in certain settings with high industrial emissions.

The accumulation and toxic effects of these poisonous elements can be markedly influenced by dietary zinc. The mechanism of the interaction is not fully understood but there is strong evidence that the most important interactions occur in the gastrointestinal tract.

The influence of insufficient or supplemental zinc intake on heavy metal absorptions and heavy metal deleterious effects may have health implications, especially in populations with deficient or marginal zinc intake. The zinc fortification of foods as a measure of protection against the toxic effects of heavy metals should be investigated further.

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