ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Trace Elements in Health and Disease: A Review.

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ABSTRACT

Trace elements are essential for normal physiological activities. They are present in minute/ trace quantities in our body and the term "micronutrients" is also used to refer to them. They are essential for many enzymatic reactions and are components of the food chain. Enzymatic reactions form the basis of metabolism (catabolism and anabolism) in many biological organisms including the human beings. When metabolism is affected as in diseased states, homeostasis is disrupted. Hence, deficiency or excess states of these elements can lead to adversities. Copper, Zinc, Chromium, Selenium, Nickel and Iodine are common trace elements present in varying amounts in both vegetarian and non-vegetarian diet. Knowledge on these trace elements, their dietary sources, recommended dietary intake, deficiency states and hazards of excessive consumption is very less, even in practicing clinicians. The process of adding trace elements to soil/ food is gaining popularity and is an effective method to increase the consumption. Throwing light in this area can help to reduce the incidence and severity of many diseases.

Keywords: Trace elements, deficiency, excess, disease

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ISSN: 0975-8585

INTRODUCTION

Trace elements constitute 0.005% of the total body weight. Estimation of these elements was difficult in earlier days. As these elements are present in minute quantities, their deficiency or excess states could not be determined precisely. But with recent technological advances, it has become easy for precise estimation of these elements. Though macronutrient deficiencies are more pronounced in the general population, thorough literature studies show that micronutrient deficiencies are more prevalent in developed as well as developing countries like India.

Measurement of trace elements:

- Trace elements can be measured in Serum, leucocytes, lymphocytes, hair, urine
- Measurement of enzyme activities
- Functional studies
- Balance studies
- Analysis of dietary intake
- Checking for alleviation

Though various methods are widely available, the most commonly followed technique is Atomic Absorption Spectrophotometry technique. Few ml of venous blood is collected in metal free tubes without the addition of anticoagulants. Serum is separated and analysed for trace elements using graphite furnace atomic absorption.

Major causes of trace element deficiencies:

- Inadequate supply
- Congenital metabolic disorders
- Inadequate intake
- Iatrogenic causes
- Metabolic diseases

It is estimated that more than 3 billion of the world's population are affected by micronutrient(trace elements + vitamins) deficiencies." Micro-nutrient Fortification"- fortification of nutrients in the soil-is a simple, inexpensive, effective strategy for increasing the bioavailability in plants and soil.

ZINC

The recommended daily Zinc intake levels 7-11 mg/dl [1]. Zinc deficiency was recognised as early as 1963. Zinc is an essential constituent in various enzymes that are needed for the normal bio-physiological processes in the body. To mention few enzymes Carbonic anhydrase, peptidase, alcohol dehydrogenase, alkaline phosphatase, polymerase, Superoxidedismutase and so on. It also plays an important role in the regulation of gene expression.

Deficiency

Recent data shows that upto 30-40% suffer from zinc deficiency. The manifestations are varied from reduction in anti-oxidant potentials, immunodeficiency's, taste and olfaction disorders, abnormal pregnancies, developmental retardation, premature ageing.

Serum Zinc / copper ratio can be used clinically to detect deficiencies of Zinc levels. Zinc / copper ratio is significantly lower in diabetic subjects in whom there is significant hyperzincuria and low serum zinc levels [2].

Excessive intake

Zinc can hinder copper absorption.

Food sources

Fortified cereals, red meat, few seafoods.

COPPER

The recommended daily Copper intake levels 1-4 mg/dl [1]. Copper is an important constituent of ATP 7A and ATP 7B genes and it is highly homologous and is the constituent of ATP- Copper transporter membrane proteins. Cerruloplasmin is the copper in the bound form. It is a constituent for lysyl oxidase, Superoxide dismutase, Tyrosinase, ascorbate oxidase.

Deficiency

Menke's disese is an inherited disorder of Cu transport from the intestine and it results in Cu deficiency leading to increased capillary fragility. Cu malnutrition can result in Low-birth –weight babies, small for gestational age infants. Also deficiency is common after gastrointestinal surgeries, prolonged parenteral nutrition, and intractable diarrhoea.

Clinical studies have shown varied levels of copper (increased or same) in the serum and decreased serum zinc levels in type II Diabetes mellitus.

Excessive intake

Copper can cause hepatotoxicity and GI disturbances [3].

Food sources

Meat, seafood, whole grain, nuts, cocoa products

CHROMIUM

The recommended daily chromium intake is 28-62 µg/dl[1]. Extensive research has thrown light on a close link between Diabetes mellitus and chromium deficiency. Large number of clinical trials has also shown that Cr in the form of chromium picolinate and zinc helps to alleviate the symptoms in type II diabetes mellitus and Gestational DM [4]. Studies have postulated various mechanisms like increased receptor phosphorylation [5], increase in AMP kinase and p38 MAP kinase activities [6] and increase receptor mRNA [7].

Oxidative stress has been linked to the etiology of the late complications in DM which can be minimised by Cr supplementation. Serum chromium varies in direct proportion to CD4+, CD25 + T cells. Though there is still much controversy regarding the role of trace elements in diabetes, Nicolas et al in their diabetic update concludes by saying that trace elements are beneficial only when they are combined together or supplemented with antioxidants and oral hypoglycaemics [8].

Excessive intake

Can lead to nephrotoxicity.

Food sources

Meat, poultry, fish, cereals

SELENIUM

The recommended daily Selenium intake is 41-168µg /dl[1]. Plays a key role in oxidative stress, thyroid hormone regulation, redox-status of vitamin C. Selenium, copper, iron, zinc are needed for the neutralisation of the free radicals.

In 2001, Mingguang Tan et al have proved in their study of 234 gestational diabetic subjects, that selenium levels were significantly lower in pregnant women with IGT and GDM[9]. Also similar findings have been reported by Douillet et al[10].

Deficiency

Carcinogenic, IHD

Excessive intake

Excessive levels can lead to hair and nail loss or brittleness.

Food sources

Fish, grain

IODINE

The recommended daily Iodine intake is 200-3000 µg/dl[1]. It is the most essential component of Thyroid hormones namely tri-iodothyronine, tetra-iodo-thyronine. Iodine deficiency disorders are spread across 130 countries affecting 2.2 billion globally.

Iodine deficiency could be due to reduced salt intake, less intake of iodine containing food or increased intake of iodine uptake inhibitors like perchlorates and fluorides. Iodine is essential for normal brain development especially in –utero and in neonates, thyroid function, maintenance of healthy breast and even prevention and protection against stomach cancer. When daily intake reduces to less than 10-20 mcg/day, it can result in goitre and hypothyroidism. In children, especially, moderate to severe I_2 deficiency results in decreased IQ by 12-13.5 points [11,12]. It is alarming to note that 31% of children world-wide do not have access to Iodised salt. Hence, pregnant women and neonates are at risk for developing iodine deficiency.

Deficiency

Cretinism with mental retardation in children and myxoedema in adults.

Excessive intake

Raise in the TSH levels

Food sources

Sea food, iodized salt, processed food

NICKEL

The recommended daily nickel intake is 0.6-1mg/dl[1] and their recommended intake is not determined in infants and children less than 2 years due to lack of suitable data. Serves as a cofactor of enzymes and plays a role in Iron absorption.

Exposure to nickel can occur via air, water and food and inhalation is the most important route through which humans are exposed to dangerously high levels during occupational exposure. Drinking water usually contains less than 10µg/L and hence very safe. Nickel gets deposited in many aquatic plants which is a leading biomarker for water pollution. Food generally having nickel content between 0.1mg/L and 0.5mg/L is safe for consumption. Hydrogenation of fats and oils, milling of flour and leaching stainless steel vessels add to the nickel content in the food stuff. Nickel toxicity is due to Nickel interference with Fe, Mn, Ca and Zn and also due to its ability to replace the metal ions in proteins and enzymes [13,14].

Serum and urinary levels are higher in exposed people than otherwise. Nickel exposure can cause variety of symptoms ranging from contact dermatitis to cancer. Though the exact mechanism is still under debate, carcinogenicity of nickel is well established. U.S. Environmental Protection Agency has classified Nickel as a well-established carcinogen due to emission of *beta* and *Gamma* particles from the radioactive isotope. It is found in abundance in nuclear reactors and fuel processing plants [15].

Excessive intake

In animal studies has proven weight loss.

Food sources

Nuts, legumes, cereals, sweeteners, soy products

MAGNESIUM

The recommended daily magnesium intake is 240-320 mg/dl [1]. It is a cofactor for various enzymes. Plays an important role in diabetes mellitus. Hypermagnesuria is a consistent finding in Type II DM. Supplementation with other antioxidants is very important in managing DM.

Excessive intake

No significant side effects

Food sources

Green leafy vegetables, nuts, polished grains, milk

MOLYBDENUM

The recommended daily intake is 35-50 µg/dl[1]. Cofactor for enzymes involved in sulphur aminoacids and purines and pyrimidines. There has been extensive research on male infertility and molybdenum. Mo toxicity is strongly associated with decreased sperm concentration as well as motility[16]. Individuals with low copper levels are more prone for molybdenum toxicity.

Excessive intake

Male reproductive toxicant

Food sources

Legumes, grains, nuts

Deficiency of micronutrients in soil and plants has been extensively reviewed in the past few years and is termed as 'hidden hunger', as it can lead to diseases in plants as well as humans. As there is lot of genetic variability within the major cereals-rice, wheat and maize, adequate supplementation of the soil with micronutrients can help in meeting their physiological requirements. Functional genomic technology including metabolite profiling fortification with Zn, Fe and Mn combined with higher yield of cereals can be implemented. Extensive literature studies show that trace elements are essentially altered in various metabolic disorders, ranging from thyroid hormonal imbalance to infertility. Whether these are consequences to the disease or they contribute to the genetic expression and mutation needs to be studied in the future.

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