Materno- Fetal Relationship of Zinc and Copper In Health and Disease

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Thesis

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By

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INTRODUCTION AND AIM OF THE WORK

Trace elements are those elements which occur in the body in very low concentrations, less than 0.01 % of body weight (Laker 82).

Interest in the nutritional importance of zinc, long ignored in human nutrition, is presently growing rapidly.

The biological role of this metal was established over a hundred years ago (Under wood 71). However it was not until 1960s that zinc deficiency was recognized in man (Prasad 61, Prasad 63).

The role of copper as an important trace element in human nutrition in health and disease, also can not be ignored.

Trace elements particularly zinc and copper have a major role in growth and development of the fetus and infant (Pabacan, et al., 81).

The possible changes in these trace elements in normal, mal nourished, high risk pregnant mothers may have an influence on the fetal growth and anomalies, consequently on neonatal and infant growth pattern.

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The aim of the present work is to find out any relation between serum levels of the mother and the newborn as regards copper and zinc trace elements, and the repercussion of some high risk deliveries on these levels.

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REVIEW OF LITERATURE

ZINC

Zinc in nature:

Metallic zinc was not discovered as early as many of the other metals, its very important use as an alloy with copper in brass manufacture antedates the earliest records of investigation.

Since zinc does not occur in an uncombined state in nature, the discovery of brass presumably was a happy accident . The name of zinc is taken from the german "of unknown origin".

The chinese probably were the first to extract zinc metal.

The element has been estimated to represent 0.004 % of the earth's crust and is 25th in order of abundance. Zinc usually occurs in combination with sulphur or oxygen.

The element has the atomic number 30 and isotopes of which Zn 65 with half life 250 day which has been most widely used for biological studies and zinc 68 with a much shorter half life 38 minutes which has been employed where this property is a desirable factor as

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in therapeutic investigations.

The presence of zinc in living organisms as an essential nutrient for plants and animals has been recognized even since it was shown by Raulin 1869 to be necessary for the growth of Aspergillus Niger. Its occurence in biological matter was first described by Raoult and Breton 1877 to be present in the human liver.

Lutz 1926 studied the distribution of zinc and he found it to be present in all organs of the rat, cat, and man.

Sources of Zinc:

Foods that are rich in zinc are beef, chicken, shell fish and whole karnel breads (Schlage, Wortberg, 72).

Commercial infant formulas have been supplemented with zinc since 1975. They were zinc deficient because zinc bound to protein is removed when the protein content of formula based on cow's milk is artificially decreased, for example Enfamil baby milk found in the market is very deficient in zinc (Evans et al., 80).

Although both Cow's and human milks are good sources of zinc, the bioavaila bility of zinc from human milk is superior because of the presence of zinc

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binding substance (Evans et al., 80).

When breastfed and formula fed infants were compared for growth parameters, the growth rate was found to be higher in breast fed infants (Uysal 81).

Zinc concentration in colostrum may be as high as 20 mg/L., with progressive lactation zinc content drops below the average of 3 mg/L. and may fall as low as 1 mg/L. or less, presumably because of deficient zinc nutrition of the mother (Evans et al., 80).

Increased calcium content of the diet accentuates the non availability of zinc phosphates also in zinc phytate complex (WHo, 73), utilization of dietary zinc (Becker, Hockstra ., 71).

Requirements:

According to calculations based on zinc conc.in increments of fat free body mass after birth, the young infant requires a retention of 0.3 mg/day or an intake of at least 1.2 mg/day.

The actual intake ranges from 2-5 mg/day in infants, under three years of life and from 5-7 mg/day in 3-5 years old children (Schlage, Wortbery , 72).

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Zinc requirements are influenced by ambient temperature which causes profuse sweating and consequent large losses of zinc in sweat and by parasitic infestation with its attendant blood and heme zinc losses (Under Wood 77).

The recommended daily allowance (FDA) is liberally set at 2 mg/day for infants under 7 months and at 5 mg/day for infants 7-12 months (Schlage, Wörtberg, 72).

Requirements for zinc increase at puberty especially in male associated with the high concentration of zinc present in the testes and accessory male sex glands especially the prostate (Maw Son et al., 53). and a deficiency of this element appears to be more common in males than females.

Bio Chemistry of Zinc:

The red and blue colors of iron and copper protèins seem to have been responsible for their early recognition and systematic study, possibly due to their lack of visible color the identification of zinc proteins has been more or less delayed.

Biologically, zinc is found to be complexed to organic ligands rather than free in solution as the metallic ion.

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The physical chemistry of zinc complexes with ADP, ATP had been extensively studied Kahn 1955

Zinc binds to the imidazole group of human serum albumin. Zinc ions at a concentration of 15 mU will form water soluble complexes with albumin, α Lipo-proteins, α glyco proteins, alkaline phosphatase, serum esterase and metal combining globulin. The B lipo-proteins and γ globulin or fibrinogen are insoluble in water under the same conditions. The proteins can be solubilized with chelating agents by the selective dissociation of zinc protein complex. In this manner, subfractions of γ globulins can be prepared Isliker 1955

In blood serum zinc exists in at least two fractions:

Firmly bound	34 %
Loosely bound	66 %

The firmly bound zinc protein, a globulin satisfies the criteria of metallo proteins, where as the loosely bound zinc protein should be defined as metallo-protein complex. The loosely bound complex appears to be concerned primarily with zinc transport Vikbladh 1951

Neither substance has been shown to exhibit enzymatic properties.

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Insulin: It has been known for many years that crystallization of insulin at pH levels near 6 may be accomplished only in the presence of Zn^{++}, Cd^{++}, Co^{++} or Ni^{++} scoh 34

Distribution of zinc in the body:

The zinc content of various tissues has been studied by many workers during the past 80 years. Lutz 26 investigated zinc content of many organs in the rat, cat and man. The data indicated that zinc occurs in all tissues of these species, varying within narrow Limits. The zinc/nitrogen ratio would be suitable for comparison since zinc is usually found in proteins. The presence of blood in the organs would be a source of error. Some refere zinc level to ash weight or day weight.

Zinc is present in human and other vertebrate organs, including man, in quantities varyigh from 10 - 200 Ug/gm koga 1935, Leiner 1941, vallee 1949.

Most organs including the pancreas contain between 20 - 30 Ug of zinc per wet tissue. Liver, voluntary, muscles and bone contain about double this amount. The zinc content of liver of newborn rats is 2-3 fold higher than that of adult animals, Within 2 weeks post partum,

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the concentration decreases to about 100 ppm which is the content of adult rat Livers . The dermal appendages of various species have been found to contain substantial amounts of zinc. The difference in organ content of different species is not remarkable, and in view of the analytical uncertainties, the detailed results add little of significant value Underwood 56.

An extensive study determined the mineral composition of whole human bodies on a fat free basis widdowson 51. The total zinc content of an adult fat free body weighing 70 Kilos veries from 1.36 to 2.32 grams.

The total iron content is 4.2 - 6.1 grams and the capper content 81 - 230 milligrams.

The distribution of Zn^{65} in the mouse and dog has been studied as a guide to the distribution of the metal in tissues .

Animals were serially killed subsequent to the injection of the isotope. The amounts of zinc introduced were negligible as compared with the total amount in the body. In both mice and dogs the liver contained the largest fraction of the injected dose early in the experiment. Over a period of 160 hours the most rapid uptake and loss was observed in liver, pancreas, Kidney

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and pituitary. Least activity was found in erythrocytes, brain, skeletal muscle, and skin. The activities of spleen, gastro - intestinal tract, adrenals, lungs, lymph nodes, brain, heart and thymus were inter mediate.

RBCs and bone were the only tissues examined which accumulated zinc. Of the administered dose of $zinc^{65}$, 6.5 % was exreted in pancreatic juice within 5 days Montgomery 43.

These data have been confirmed and elimination of the metal in bile has also been found . Since carboxy peptidase of pancreatic juice is a zinc metallo-enzyme at least a fraction of this zinc elimination is accounted for by this enzyme, though other zinc enzymes may also be found to contribute to the total amount of zinc in pancreatic juice. The isotope crossed placentae of rat and dog, more than half the dose retained is transferred to the young through the milk within 96 hours Feaster 55

The male genital organs and semen, the pancreas, the tissues of the eye and the liver and body fluids have been investigated intensively and it was found that there is a high zinc content of horse testis, seminal vesicles of swine and rat epididymis, as well as human prostate. . Some trials were made for treatment of

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some cases of man sterility by intra prostatic injections of some zinc compounds. There are about (5 - 30 Ug) of zinc in the human epididymis and seminal vesicles per gram of wett weight.

The activity of carbonic conhydrase increase smultaneously with increase of the zinc content of the prostate. Diminished concentration of zinc is found in cases of prostatic hypertrophy and prostatitis ..
Mawson 52

Zinc deficiency of rats, induced by a diet containing less than 0.5 Ug zinc per gram, results in degeneration of the testes, hypoplasia of the coagulating glands, seminal vesicles and prostate and relative or complete decrease in the number of sperms in the epididymis. All changes produced by zinc deficiency, except the testicular atrophy, were reversed when zinc was restored to the diet
Millar 52.

The effects of testosterone and gonadotropin administration to these zinc deficient animals suggested a diminished production of these hormones as a result of zinc deficiency. Gonadotropin specifically increased size of prostate, seminal vesicles and coagulating glands, testis and epididymis, and further induced an increase in zinc content and rate of uptake of zinc by

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