SELENIUM

Pages with reference to book, From 90 To 94

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Although many advances have been made in recent years towards understanding the role of trace elements in human health, the clinical detection of deficiencies is often extremely difficult because of(a) the lack of specific signs of symptoms in the early phase of disease, (b) the lack of specific, precise and reliable assays for the measurement in systems in which the element is involved, (c) problems at the nutritional and cellular level involving the interaction of element with element or element with other nutrients.

Role of Selenium

Selenium, originally regarded as being a very toxic element, was found to be an essential trace element in humans and animals in 1957, and an integral part of Factor 3, an agent active against liver degeneration[1]. In 1973 erythrocyte glutathione peroxidase was found to have a selenium cofactor[2] and the enzyme was in fact identical to Factor 3. Glutathione peroxidase (GSHPx) catalyses the reduction of lipid peroxides., (ROOH) by glutathione (GSH) [3].

200H + 2GSHPx, ROH + H2O + GSSG

Lipid peroxides disrupt cell membranes and macromolecules such as DNA[4]. GSHPx also prevents the accumulation of prostaglandin G (essential in the inflammatory response) and regulates prostacycline biosynthesis, which inhibits the aggregation and adhesion of platelets to the lining of blood vessels[5]. In tissue homogenates from the rat, thirteen selenium containing proteins or protein subunits have now been identified, including the subunit of GSHPx. Except for GSHPx, their functions are unknown, but presumably have biological importance because in an inadequate selenium intake, these have priority for the selenium over GSHPX (Ref.6 and private Communication).

Bloavailability and metabolism

Plants provide the principle source of selenium mostly as selenomethionine in the food chain and thence as selenomethionine or selenocystine in the meat, fish and dairy products[7]. Water and air contribute little except in regions of heavy pollution[8]. The element is available to plants mostly as selenate from the soil especially when alkaline, and the soil content depends on that of the rocks from which it is formed. However, it is readily leached from the surface. Selenium distribution is ubiquitous but uneven resulting in regions of very low to very high levels, the major factors contributing to this are the nature of the parent rock, rainfall, climate, pH and soil composition[9,10]. Selenium is readily absorbed in the gastrointestinal tract but may also be absorbed by the respiratory tract and skin in environmental exposure. Excretion is mainly by the kidneys, which exert a degree of homeostatic control, and a small amount appears in the faeces. There appears to be no storage form although levels are higher in the liver and kidneys than in other tissues[11]. Selenium ingested as selenomethionine is partly catabolised to release selenium to the central selenium pooi and the remainder goes to the tissues as selenoproteins via re-conversion first to selenomethionine. That in the central pool becomes the cofactor of glutathione peroxidase upto a saturation level and after that excess is excreted but that in the tissues can increase steadily with increasing dietary intake. Selenocysteine and inorganic selenium go to the central poor only and not towards the formation of selenoproteins in the tissues[12]. Blood selenium levels reflect dietary intake and a safe and adequate intake of American adults is generally accepted as 50-200 ug daily[13]. In Great Britain, a mean intake of 60 ug/day has been reported[14] and a normal range of 9.3-15.3 ug/dl in whole blood. Extremes maybe encountered e.g. in the Keshan district of China prior to 1979, the mean intake was only 11 ug/day[15] with a mean level of 2.1 ug/dl[16] but in

Hubai province, the mean intake was 4490 ug/day[16].

Selenium status

The determination of selenium status is difficult. GSHPx activity in blood platelets gives the most accurate assessment as platelets have a rapid turnover[17], a high selenium content[18], the GSHPx is depressed in selenium deficiency[19] and responds quickly to dietary intake[20]. Also, the activity correlates well with selenium and GSHPx activity in the liver[21]. If selenium is administered to correct selenium deficiency, platelets GSHPx activity give a measure of selenium bioavailability, blood or plasma selenium levels give an estimation of selenium retention, and after supplements have been discontinued, platelets GSHPx gives an assessment or tne convertability of tissue forms to biologically active selenium[22]. The diet of selenium deficient Finnish men were supplemented with 200 ug/day of selenium as selenium rich wheat, selenium rich yeast or as sodium selenate for 11 weeks. Plasma selenium increased in the wheat and yeast groups but plateaued after 4 weeks at 11 ug/di in the selenate groups. Platelets GSHPX increased and plateaued after 4 weeks in the wheat and selenate groups but continued to slowly increase in the yeast group. At 10 weeks in all cases, platelets GSHPX was higher but more so in the wheat and yeast group[22]. Selenium is thus more bioavailable in the organic forms, especially in yeast.

Selenium toxicity (Selenosis)

This is rare, the classic example being that which occured in Hubei province, China[23] when after having exhausted the local brushwood, the population burnt the nearby highly seleniferous coal in their homes as well as on the field as a fertiiser. The mean daily[16] intake rose to 4990 ug (recommended 50-200 ug[13]) and the resulting endemic selenosis was manifested commonly by a generalised loss of hair and nails.

Selenium deficiency

This is becoming apparent much more than was thought until fairly recently. Clinical symptoms may vary from none, for reasons unknown, to the well documented Keshan disease[15], an endemic cardiomyopathy and Kashin-Beck disease[24], an osteoarthropathy, both occurring in Heilongjiang province, China, until the distribution of sodium selenite supplements to the population. In some cases the selenium status in Keshan disease was actually higher than in other symptomless cases found in some other countries. However, many other diseases and conditions have been associated with selenium deficiency some of which have responded to supplementation.

Cardiovascular disease

Low serum selenium levels have been linked to an increased incidence and risk of cardiovascular disease[25] exemplified by the fact that in 1970's, E. Finland had the world's highest mortality from coronary heart disease and atherosclerotic cardiovascular disease for men[26], that the selenium content of the soil is very low in that area and that the intake had been only 20-30 ug/day[27]. After acute myocardial infarction low plasma and RBC selenium levels had been found together with high RBC GSHPx activity. In these cases low selenium levels in toe-nails showed that for approximately one year before infarction, the selenium status had been low[28]. There was no relationship between serum levels and the severity of infarct or where infarct had occurred[29]. Heart tissue from by-pass surgery had low serum, blood and RBC selenium levels and serum levels correlated well with those in the heart tissue (r = 0.604) and blood levels with those in the ejection fractions (r 0.303). No correlation was found involving RBC levels showing that the turnover rate for selenium in tissue is similar to that in serum but greater than in RBC\'s[30].

Liver disease

Selenium deficiency produces not only lesions in the heart, but also in the liver and in skeletal muscle[31]. Serum lipid peroxides were found to be elevated in liver in deficiencies of selenium and

vitamin E, e.g. in alcoholic cirrhosis, but no changes were found in blood GSHPx activity[32].

Other diseases and conditions

There is an inverse relationship between the rate of cancer mortality and selenium bioavailability in forage crops[33]. Low plasma selenium levels have been found to cause depression of the immune system and occur in many bacterial infections but rarely in viral infection[34]. Low blood or plasma levels of selenium and of GSHPx in blood have been found in multiple sclerosis[35], rheumatoid arthritis[36], hyperthyroidism[37], endemic goitre[38], cystic fibrosis[39], and in Crohn's disease (but not in ulcerative colitis) and in perianal complications of inflammatory bowel disease[40] Selenium deficiency has also been associated with eye lens cataracts[41], infertility[42], anaemia[43]. glucose intolerance[44] and increased plasma LDL-cholesterol[45], a cardiovascular risk factor. Many of the above conditions may be alleviated by selenium supplementation, sometimes by huge doses e.g. upto 500 ug/day may be required in some Crohn's cases. Cases of pseudoalbinism in children[46], alleviated by selenium supplementation and cardiomyopathy in adults[47] have arisen in patients on long term total parental nutrition. Zinc and copper are added to such solutions but selenium and other trace elements should also be added because of such deficiencies arising[48]. Similarly, these should be added to the special diets in phenylketonuria and maple syrup urine disease as selenium deficiency has been reported[49]. Renal failure patients on haemo or peritonealdialysis can develop selenium deficiency[50] most likely as a result of protein malnutrition as selenoproteins (other than GSHPx) are important in body metabolism[6].

Trace Element Interactions

Lead and tin can induce anaemia by inhibiting the activity of Laminolaevulinic acid dehydrogenase, involvedin one of the steps of haem-biosynthesis. Selenium supplements can nullify the effect of lead but not that of tin[51]. Mso selenium toxicity can be reduced by lead or tin[51]. Similarly, selenium antagonises the effect of arsenic[52], mercury[53], cadmium[53], copper[54], silver[55] and zinc[56]. Treatment of cancers caused by selenium deficiency by the administration of selenium can be inhibited by zinc[57].

Age, pregnancy and lactation

Plasma, serum selenium and RBC GSHPx activity in neonates and infants increase with age after an initial drop between 60-90 days[58]. In adults, serum selenium levels decrease with age and also with haematocrit[59]. Low birth weight babies were found to have lower plasma selenium levels and reduced plasma GSHPx activity compared weight normal new borns and the hidden danger of extremely low plasma levels may arise if parentally fed without selenium supplements[60]. Plasma selenium levels are reduced in pregnancy[61]. Dietary selenium intake influences the concentration in milk and is sufficient in North America women[62] but in many parts of the world this may not be so e.g. in Nepal, blood and milk selenium levels are much lower than in USA[63]. Colostrum levels are higher than in mature milk and GSHPx activity in mature milk is greater when the infant had been pre-term than when term[64].

Dietary supplementation

E. Finland had the world's highest mortality rate from coronary heart disease in men[26], the dietary intake of selenium being only 20-30 ug/day[27] as against the recommended level of 50-200 ug/day[13] and that in USA of about 75 ug/day[65]. In 1975 Finnish soils were shown to be low in selenium[66]. Between 1975 and 1984 there was a high correlation between serum levels and selenium intake ($r = 0.89$) with rises in both in years when the import of grain was necessary[67]. In 1969 Finland had been one of the first countries to supplement animal feed with selenium to combat the deficiency in farm animals[68] and in 1984, the decision was made to supplement fertilisers with sodium selenite[69] which became effective in the 1985 growing season. This effectiveness was shown when in 1986 the mean

selenium intake of the population had risen from 39 to 92 ug/day and the serum range from 4.6 - 9.4 to 8.4 - 12.4 ug/dl[70], the USA value being 10.0 14.0 ug/dl[71]. There is evidence that in some other countries, selenium deficiency may exist on a national scale. In Belgium, in a trial, 100 ug/day of selenium as selenomethionine was given and serum levels rose from 6.0- 10.5 to 11.1-11.9 ug/dl[72]. Possibly the dietary intake of 50-60 ug/day is too low. In New Zealand the mean daily intake is only 25 ug[73] and the serum range 2.8-6.8 ug/dl[74]. levels rising when grain is imported. Among those who do not eat chicken and fish, the daily intake can be as low as 4-13 ug/day and compares with those suffering from Keshan disease in China with 4-11 ug/day intake[75]. Surprisingly, neither in Belgium nor in New Zealand are any deleterious effects apparent, for unknown reasons. Clearly, many further investigations are required.

Selenium and Pakistan

Except in parts of China and Venezuela, nothing is known of the dietary status of selenium in any developing country. In view of the high incidence of cardiovascular disease, hyperlipidaemias and diabetes mellitus, one could expect to find at least areas of low selenium status among our population. Almost the whole population may even be deficient, as was found in New Zealand[73], if we did but know it. In view of the high blood lead levels among the urban population[76], one might expect selenium bioavailability to be depressed. Conversely, a modification of the effects of lead might occur if the selenium status is normal or high[51]. Lead levels should be lower in rural areas and so this factor may not apply there. The absorption of selenium and iron from the diet may antagonise each other as does selenium versus zinc[56,57]. Supplements of iron or zinc to correct deficiencies of these elements may depress the absorption of selenium from the diet. Pan chewers may have low selenium status[53]. (Cadmium occurs in pan and lead appears to be absorbed from the metal foil when used). If wide spread selenium deficiency does occur, selenium supplements could be given to affected populations, or better still to agricultural fertifisers in those areas. This may result eventually in a decrease in one or more of the above mentioned diseases. A fuller understanding of interelement interaction may re-emphasize the need for the introduction of lead free petrol or a more careful consideration of dietary supplements e.g selenium supplementations may need to accompany iron supplementation for anaemias and the use of pan may need discouragement.

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