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**Selenium; A Clinical Review Of An Essential Antioxidant Trace Element
In The Elderly**

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ABSTRACT

Background

Antioxidant trace elements are those essential trace elements that participate in the detoxification of free radicals thereby reducing oxidative stress. Old age comes with increased oxidative stress while chronic diseases common in old age are also linked in parts to oxidative stress.

Aim

This narrative review is intended to improve the general knowledge of selenium among clinicians attending to the elderly.

Methodology

A PubMed search for published works on selenium, trace elements, antioxidants and the elderly over the past 14 years (2011-2025) was done.

Result

Antioxidants take part in scavenging excessive reactive oxygen and nitrogen species hence minimizing the cellular damaging effects of these reactive species. Antioxidants capture and inhibit the formation of free radicals and also chelate metal ions that catalyze the free radical chain reactions. Antioxidant trace elements, including selenium, detoxify free radicals mainly by being constituents of metalloprotein enzymes that detoxify reactive species. Selenium

is a constituent of glutathione, glutathione peroxidase and many selenoproteins that scavenge free radicals. Depletion worsens the outcome of chronic diseases such as cardiovascular diseases, neurodegenerative diseases, osteoporosis, cancers, diabetes mellitus, etc, which are common in old age. Conversely, an excessive level of selenium is toxic. It is, therefore, necessary to maintain a normal balance of selenium in the elderly for better outcome of chronic diseases in this venerable population.

Conclusion

This review attempts to emphasize the role of selenium in metabolism as well as in chronic diseases common in the elderly reminding physicians that the care of the elderly should include ensuring that the micronutrient, selenium, is not deficient in order not to worsen the outcome of chronic diseases common in the elderly.

Keywords: Selenium, Elderly, Micro-Mineral, Antioxidants

Introduction

Trace elements are those elements existing in natural or perturbed environments in small amounts but are pivotal to healthy living while excess bioavailability has toxic effects to the body ¹. They are chemical micronutrients which are needed in minute quantities to maintain the integrity of the body's physiologic and metabolic system ¹. The antioxidant trace elements are those trace elements that take part in

mopping tissue free radicals. Their serum levels are affected by several disease processes, including those diseases common in old age, and in turn these trace elements may modify the progress of disease processes ^{2,3,4}. Food is the chief source of these micronutrients, other sources being water and by inhalation. Nutritional deficiencies are common in the elderly and deficient levels of micro-minerals

have been severally reported in the elderly ^{5,6}.

Trace Elements Classification

In 1973 the World Health Organization (WHO) classified 19 trace elements into 3 groups ^{1,7} which are :

1. Essential trace elements comprising zinc (Zn), copper (Cu), selenium (Se), chromium (Cr), cobalt (Co), iodine (I), manganese (Mn) and molybdenum (Mo).
2. Probably essential trace elements comprising cadmium (Cd), nickel (Ni), silicon (Si), tin (Sn), vanadium (V) and aluminium (Al).
3. Potentially toxic elements comprising gold (Au), mercury (Hg), Arsenic (As), lithium (Li), and lead (Pb).

While in 1981 Frieden classified trace elements based on the quantities they occur in living tissues into 3 groups much similar to the WHO classification ^{1,8,9,10}:

1. Essential trace elements: boron, cobalt, iodine, iron, manganese, molybdenum and zinc.
2. Probably essential trace elements: chromium, fluorine, nickel, selenium and vanadium.
3. Physically promotive trace elements: bromine, lithium, silicon, tin and titanium

Therefore, selenium is classified as essential trace element by the WHO but probably essential trace element by the Frieden's classification.

Antioxidant Trace Elements

Antioxidant trace elements are those essential trace elements that participate in the detoxification of free radicals thereby reducing oxidative stress. They take part in scavenging excessive reactive oxygen and nitrogen species hence minimizing the cellular damaging effects of these reactive species. Antioxidants capture and inhibit the formation of free radicals and also chelate metal ions that catalyze the

free radical chain reactions¹¹. The antioxidant trace elements detoxify free radicals mainly by being constituents of metalloprotein enzymes that detoxify reactive species^{11,12}. These essential trace elements include selenium, zinc, copper, manganese and iron. Selenium is a constituent of glutathione and many selenoproteins that scavenge free radicals. It is also a component of the antioxidant enzyme, glutathione peroxidase^{13 - 16}.

Selenium

Selenium was discovered by J.J. Berzelius in 1817 and was initially described as a toxin but was later

found to be an essential micro-nutrient in the 1950s¹³. In nature selenium occurs as a combination of inorganic (in water and soil) and organic (plants) forms. Its content in crops depends largely on the selenium content of the soil where the crops are grown. Food is the main source of this antioxidant trace element to man as the organic form is better absorbed than the inorganic form present in water¹⁷. The total body selenium is 10 to 20 mg in a healthy adult depending on location and age¹⁷. The average daily requirement is 50 – 100µg in adults.

Selenium Metabolism

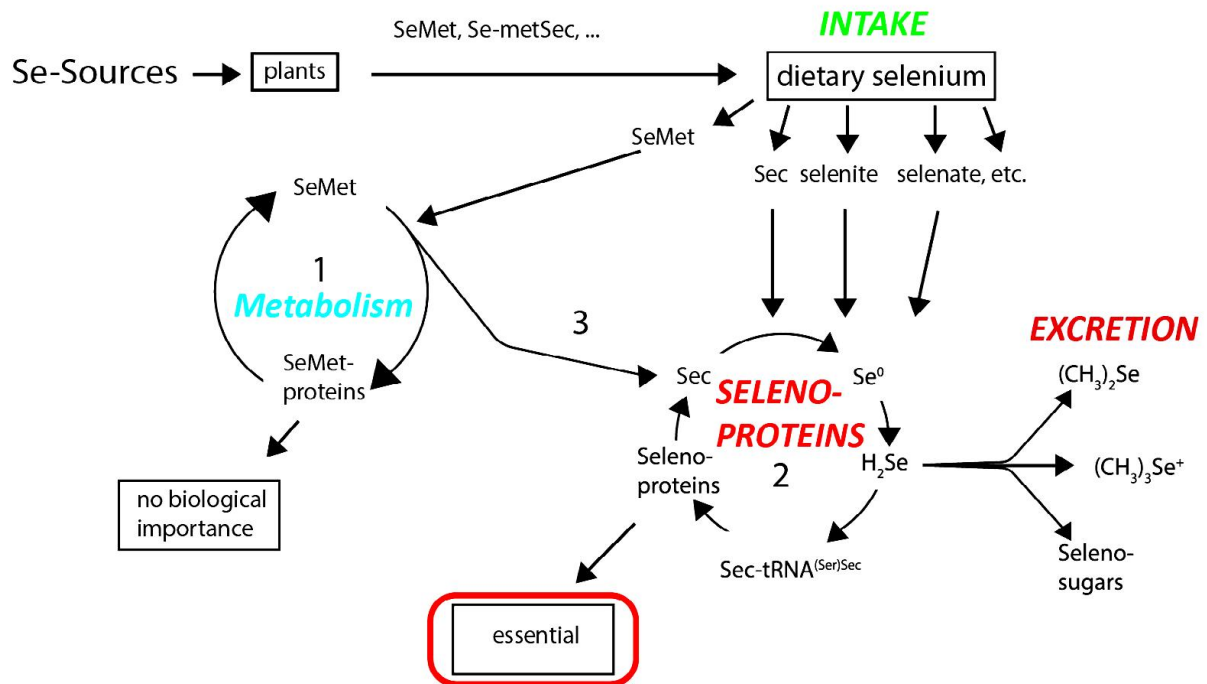


Diagram illustrating the metabolism of selenium in humans ¹⁸

After absorption in the small intestine, selenium is transported to the liver where it is incorporated into amino acids as selenomethionine (Se-Met) and selenocysteine (Sec) to form the antioxidant glutathione and selenoproteins (SePs). Se-Met and Sec are formed by the substitution of the sulphur atom of methionine and cysteine respectively with selenium. Selenoproteins are formed by the subsequent incorporation through very complex mechanisms into the polypeptide chain or by the non-specific substitution of sulphur in

methionine of a polypeptide or even by selenium binding non-covalently to selenium binding proteins ¹⁷. Selenoprotein P is the selenium transport protein to peripheral tissues ¹⁵. There are 25 selenoproteins known in the mammalian tissue ^{15,19}. Of these selenoproteins, glutathione peroxidases (GPX) 1, 2, 3, 4 and 6 and thioredoxin reductases 1, 2 and 3 are very potent antioxidant enzymes in different parts of the tissue ^{15,19}. Glutathione peroxidase 1 (GPX1) is the major GPX species in

the cytosol, GPX2 in gastrointestinal tract, GPX3 in plasma, GPX4 in phospholipid layer GPX6 in the olfactory system ¹⁹. Other selenoproteins have synthetic, regulatory or antioxidant functions.

Selenium Depletion and Neurodegenerative Diseases in the Elderly

Neurodegenerative diseases are common in the elderly. Free radical damage to neuronal cells is one of the theories of neurodegenerative disease. About 20% of total selenium in the brain is incorporated in glutathione peroxidase enzymes which break down hydrogen peroxide, organic peroxides and phospholipid peroxide to alcohol or water by using glutathione, mercaptoethanol, cysteine or other protein thiols as reducing co-substrates ¹⁷. Accumulations of these free radicals have very damaging effect to the brain cells partly implicated in neuronal degeneration leading to common diseases in the elderly such as Alzheimer's

dementia (AD) and Parkinson's disease. Serum selenium was reported to have a characteristic pattern that could aid early diagnosis of AD ²⁰. It tended to increase in patients with subjective memory complaint (SMC) and then progressively to decrease in patients with mild cognitive impairment (MCI) and AD ²⁰. In that publication 22 elements were profiled and zinc, manganese and iron showed the same pattern with selenium (increase in patients with SMC and progressive decrease in patient with MCI and AD). Alzheimer's disease tend to progress from SMC to MCI to AD. This distinctive signature pattern (of increase in SMC and progressive decrease in MCI and AD) could help in pre-clinical staging and early diagnosis of AD if these trace elements are monitored in the elderly ²⁰.

Selenium Depletion and Cardiovascular Diseases in the Elderly

Hypertensive crises syndrome and hypertensive heart failure were among the most common geriatric emergencies in a rural hospital in South-Eastern Nigeria ²¹. Aging comes with increased risk of hypertension, hypertensive heart failure and atherosclerosis. Essential trace elements and free radicals play key roles in myocardial damage and atherosclerosis, with the trace elements reducing free radical cellular damage ^{22,23}. Selenium is reported to be decreased in heart failure and such level may have key role in the pathogenesis of myocardial damage in heart failure irrespective of the aetiology ²². Selenium depletion was observed in 70% of heart failure patients with depletion associated with lower exercise capacity, lower quality of life and worse prognosis ²⁴. Supplementation in the elderly with heart failure improved symptoms, improved left ventricular ejection fraction and also improved lipid profile ²⁴.

Elderly heart failure patients with selenium deficiency had worse clinical signs and symptoms of heart failure, poorer exercise capacity as well as lower quality of life ²⁵. Selenium deficiency probably impaired mitochondrial function and oxidative phosphorylation as well as increased myocardial cellular reactive oxygen species leading to myocardial damage ²⁵. Meta-analysis of observational studies showed a reduced risk of cardiovascular disease and mortality in a physiologically high selenium status compared to low selenium status ²⁵. However, excessive intake should be avoided due to toxicity in too high levels.

The relationship between selenium and cardiovascular disease is still complex but most data suggests that deficiency of selenium increases the risks for cardiovascular diseases ¹⁹. Some authors caution unguarded supplementation as supplementation in patients with normal selenium levels pose increased cardiovascular risk ²⁶. An optimal selenium status in

the elderly is important to minimize myocardial damage and atherosclerosis.

In two groups of post-menopausal Indonesian women, the hypertensive group had lower dietary selenium intake than the normotensive group supporting the hypothesis that selenium may have protective functions in cardiovascular system of elderly women ²⁷.

Selenium Depletion in the Elderly and Cancers

Over 83% of very old adults (85 years of age and over) were reported to have low levels of selenium ²⁸. Among elderly subjects in a prospective study, mortality rate were higher among those with low serum selenium levels, suggesting that selenium plays a role in health maintenance in aging individuals ²⁹. During ageing, there is accumulation of oxidized proteins and macromolecules, either due to increased oxidative stress or decreased antioxidant activities or both ^{26,30}. The reduced expression of

the antioxidant selenoproteins apart from nutritional deficiencies partly accounts for the decreased antioxidant activities ^{19,29}. Free radical-induced deoxyribonucleic acid (DNA) damage lead to genomic instability, DNA mutations and consequent tumour initiation and progression leading to the development of carcinomas in the elderly ¹³.

Serum levels of selenium showed progressive decline from healthy subjects having normal levels to patients with pre-malignant oral lesion such as oral leukoplakia to patients with malignant lesions such as oral cancer ¹. The element was reported to be decreased in Polish pancreatic cancer patients and Nigerian women with invasive cervical cancer ³¹.

Baseline selenium levels decreased with increasing age in colorectal cancer patients, the elderly with colorectal cancer having lower selenium values with higher risk to life ³². Selenium depletion among a cancer cohort was worst in

pancreatic cancer, then colorectal cancer and least in breast cancer ³². Supplementing with 600µg daily oral selenium during cancer treatment effectively corrected selenium deficiency in most cases and improved global quality of life, physical and emotional functioning and also reduced fatigue ³². These improvements waned over 3 months but persisted longer when selenium levels did not decrease ³². Therefore, although the maximum allowable daily dose of selenium is 300µg, in cancer treatment in the elderly, selenium supplementation is not just important but daily doses may be increased with beneficial outcome.

Selenium Depletion in Elderly and Osteoporosis

One of the features of old age is diminished gonadal hormone production (primary hypogonadism) and consequent degeneration of the protein backbone of the bone leading to osteoporosis. Osteoporosis is a major cause of long bone fractures in post-

menopausal women causing poor quality of life. Excessive intracellular free radicals are believed to participate in the development of osteoporosis by retarding the differentiation of bone marrow stromal cells into osteoblasts ¹⁴. There are findings supporting the role of free radicals in promoting bone resorption as osteoporotic bone tissue demonstrated higher levels of lipid peroxides and hydrogen peroxide but lower activities of the antioxidant enzymes superoxide dismutase (SOD), GPX3 and glutathione-S-transferase when compared to non-osteoporotic bone tissue ¹⁴.

Osteoporosis, osteoporotic fractures and osteoarthritis are common in the elderly and have been linked in part to selenium deficiency ³³. Elderly subjects with osteoporosis have lower serum selenium levels compared with elderly subjects without osteoporosis, signifying lower antioxidant status ^{34,35}. On the contrary, elderly subjects with high

serum selenium had higher bone mass density for femoral neck and lumbar spine ³⁴. A meta- analysis of both prospective and retrospective studies showed that serum selenium correlates with bone mass density and negatively with osteoporotic fractures ³⁵. Selenium based biomaterials or nanoparticles have been shown to prevent and treat osteoporosis and osteoarthritis in the elderly without increased toxicity which can be associated with over-supplementation ³³.

Therefore, maintaining a healthy selenium status in the elderly is important to prevent progressive degeneration of the protein backbone of the bone.

Selenium Depletion in the Elderly and Diabetes Mellitus

Selenium deficiency causes an increased risk and progression of diabetes mellitus, especially type 2 diabetes mellitus because of its effect in antioxidant defense and insulin signaling. Depletion of this micro-mineral impair the function

of selenoproteins causing oxidative stress, consequent oxidative pancreatic β -cell damage and reduced insulin sensitivity, thereby contributing to the sustenance of hyperglycaemia. Supplementation of selenium may be beneficial in deficiency but excessive levels may be toxic highlighting the importance of maintaining a proper balance of the trace element ^{37,38}.

In an elderly French population, male subjects with low serum selenium were at higher risk of having type 2 diabetes mellitus compared to those with optimal selenium levels ³⁹. Balanced selenium is crucial in the elderly patients to reduce the risk of type 2 diabetes mellitus as there exists no simple linear relationship between selenium levels and type 2 diabetes mellitus ⁴⁰.

The risk of diabetes mellitus is best represented in a wide dose-dependent manner, getting often the U-graph, some argue that both too low and too high selenium intakes

could increase the risk of diabetes ⁴¹. Therefore, taking more selenium is not necessarily better in reducing disease, but its baseline value should be considered to avoid over-supplementation ⁴¹.

Selenium Depletion in Human Immunodeficiency Virus Infection

Selenium deficiency was found to be an independent predictor of survival in HIV infection ⁴¹. Supplementation of this mineral increased serum concentration by 50% and reduced coronary heart disease risk by 24% (even though this is inconclusive) and also reduced symptoms of heart disease although it did not reverse immunological and hematological parameters ⁴². Another study showed that selenium deficiency worsened cardiovascular risk factors in healthy Saudi males ⁴³. Another team of researchers suggested that selenium supplementation in HIV-infection could be of great interest in protecting cells from oxidative stress and improve survival ⁴⁴. Poor antioxidant status and deficiency of

micronutrients are common in HIV infection ⁴⁵. High oxidative stress consequent on selenium depletion and oxidative stress due to co-morbid chronic diseases common in old age impacts negatively on the outcome of HIV infection in the elderly ³⁴.

Conclusion

Selenium depletion is common in old age. Depletion worsens the outcome of chronic diseases that are common in the elderly such as neurodegenerative diseases, cardiovascular diseases, cancers and osteoporosis. During cancer treatment in the elderly, high dose supplementation of selenium may improve quality of life. While treating the elderly patients with heart failure and other cardiovascular diseases, maintaining a normal selenium status through supplementation will also improve the quality of life. In old age, selenium supplementation could prevent osteoporosis and reduce osteoporotic fractures and

osteoarthritis. Daily oral doses of 50 – 100 µg will avoid or minimize depletion without over supplementation which could be toxic. In pancreatic carcinoma, daily doses could be increased to the maximum allowable in the region.

Study Limitation

This review considered only open access articles.

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