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ROLE OF SILICON IN KIDNEY, CARDIOVASCULAR, BONE HEALTH AND IMPLANTS IN HUMANS – A MINI REVIEW

Natarajan M.[1], Selvam V.[2] and Dr. Swaminathan S.*[3]

[1]Deputy Quality Manager, Techmed Health Centre and Diagnostic Pvt Ltd. Siva Building, No.1, Krishna Street, North Usman Road T. Nagar, Chennai - 600 017.

[2]Quality Manager, Techmed Health Centre and Diagnostic Pvt Ltd, Siva Building, No.1, Krishna Street, Off North Usman Road, T. Nagar, Chennai - 600 017.

[3]Director of Laboratory Services and Consultant Biochemist, Techmed Health Centre and Diagnostic Pvt Ltd, Siva Building, No.1, Krishna Street, Off North Usman Road, T. Nagar, Chennai - 600 017.

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***Corresponding Author**
Dr. Swaminathan S.
Director of Laboratory Services and Consultant Biochemist, Techmed Health Centre and Diagnostic Pvt Ltd, Siva Building, No.1, Krishna Street, Off North Usman Road, T. Nagar, Chennai - 600 017.

ABSTRACT

Silicon (Si) is the second most abundant element in earth's crust next to oxygen. Although a neglected element, it has many applications in many diverse fields, from construction industry to the most advanced computer components as well as in human health and diseases. Silicones which are products manufactured when Si is combined with carbon, hydrogen and oxygen is the form medically used for many human health, especially in implants. Silicon also plays significant role in health and diseases of renal, cardiovascular, bone metabolism and breast implants. Research done in the past has identified the implications of silicon in Kidney, Cardiovascular, bone and implants for humans. This mini review highlights a condensed research findings done during the past two decades on the beneficial/toxic effects of silicon in the above mentioned organs. There are lacunae about silicon in other areas of human health such as diabetes, endocrine, Infertile and reproductions. More research is required in this field to understand the beneficial effects of this important mineral.

KEYWORDS: Silicon, Kidney, CVD, MBD, Implant.

INTRODUCTION

SILICON IN GENERAL HEALTH

Si is the 14th element on the periodic Table of elements and is the second most abundant element next to oxygen. It is a metalloid having properties of both metals and non-metals. Silicon readily binds with oxygen and the naturally occurring silica is silicon dioxide or silica, known as quartz and is the most common component of sand.

Si is the key ingredient in bricks, concrete and glass and the element is used to make enamels, pottery and ceramics. Its other uses in industry include semiconductor for electricity and microchips. The Silicon Valley is named after the extensive use of Si in computers, electronic components and semiconductors and chips. Silica has widespread industrial applications including the use as food additive, anti caking agent, clarify beverages, control viscosity, antifoaming agent, dough modifier and as expedient in drugs and vitamins.

The other uses of Si for human health include implant device, contact lenses, bandages and varieties of other personal use products such as shampoos, shaving cream, lubricants, toys, kitchen wares. Si has many applications for human health as a boon for weak bones in osteoporosis, heart disease, strokes, for hair and nail growth as well as in digestive disorders. It increases the overall benefits of vitamin D, glucosamine, strong and flexible joints glowing skin, stronger bones and strengthening of connective tissues.

Orthosilicic acid is the form predominantly absorbed by humans and is found in numerous tissues, including bones, tendons, aorta, liver and kidney. Data from research suggests that silica is essential for health although no recommended daily intake has been fixed.

The deficiency symptoms of Si are quite apparent as they are closely associated with connective tissues. Deficiency induces deformities in skull and peripheral bones, poorly formed joints, reduced content of cartilage, collagen and disruption of mineral balance. In the femur and vertebrae, very little toxicity data exist regarding aqueous silica consumption.

The sources of Si include apples, cereals, raw cabbage, peanuts, carrots, onions, cucumber, pumpkin, fish, unrefined grains, oats, almonds and orange. High quantity is found in hard water.

Very little toxicity data exist regarding aqueous silica consumption due, in part, to the lack of anecdotal reports of toxicity and general presumption of safety. Many forms of silica exist in nature and compelling data support myriad beneficial effects of silica in water.[1]

Although emerging research is promising, much additional, corroborative research is needed particularly regarding specialized health-promoting forms of silicon and its relative bioavailability. Orthosilicic acid is the major form of bioavailable Si whereas thin fibrous crystalline asbestos is a health hazard promoting asbestosis and shows significant impairment of lung function and increased cancer risk. It has been proposed that relatively insoluble forms of silica can also release small but meaningful quantities of silicon into biological compartments. For example, colloidal silicic acid, silica gel, and zeolites, although relatively insoluble in water, can increase concentrations of water-soluble silica and are thought to rely on specific structural physicochemical characteristics. Collectively, the food supply contributes enough Si in the above mentioned forms that could be absorbed and could significantly improve overall human health despite the negative perception of silica as a health hazard.[2]

On the skin, it is suggested that Si is important for optimal collagen synthesis and activation of hydroxylating enzymes, improving skin strength and elasticity. Regarding the benefits for hair, it was suggested that a higher Si content in the hair results in a lower rate of hair loss and increased brightness. For these beneficial effects, there is growing interest in scientific studies evaluating the efficacy and safety of using dietary supplements containing Si. Its use aims at increasing blood levels of this element and improving the skin and its annexes appearance. There are different forms of Si supplements available and the most important consideration to be made in order to select the best option which is related to safety and bioavailability. Si supplements are widely used, although there are wide variations in Si bioavailability, ranging from values below 1% up to values close to 50%, depending on the chemical form of Si.[3]

In a study, the mean Si intake was 18·6 mg/day and did not vary significantly across the 2 years of investigation. Cereals provides the greatest amount of Si in the diet (about 30%), followed by fruits, beverages (hot, cold and alcoholic beverages combined) and vegetables; together these foods provided over 75% of Si intake. Si intake in the UK appears to be consistent with those reported previously for elderly women in Western populations, but lower than those reported for younger women or for men.[4]

The mean Si intake In men in the original Framingham and Framingham off-spring cohorts were significantly higher than those in women (in the 2 cohorts). Si intake decreased with age. The major food sources were beer and bananas in men and bananas and string beans in women. Si is readily available from foods; a mean of 41% of the ingested Si was excreted in urine. The Si content of the foods consumed was significantly correlated with urinary silicon excretion. Solid foods are a major source of available Si. The association between dietary Si intake and bone health should now be investigated.[5]

SILICON AND KIDNEY DISEASES

Silica has been associated with end stage kidney disease and kidney dysfunction. Calculated Glomerular filtration rate, history of kidney disease or chronic dialysis, elevated serum creatinine, and stages of Chronic Kidney Disease (CKD) Among silicoses have been identified in Michigan's Silicosis Surveillance System. Individuals with silicosis have an increased prevalence of kidney disease. More researches are required to define the pathological changes associated with silica exposure to understand the causes of silica's adverse effect on the kidney.[6]

Occupational exposure to silica may be associated with CKD. Most studies have been conducted in occupational cohorts with high levels of exposure but with small numbers of cases. A positive relationship exists between occupational silica exposure and CKD. A dose-response trend of increasing CKD risk with increasing duration of silica exposure was observed and was particularly strong among nonwhites.[7]

Plasma Si levels are higher in patients with End-Stage Renal Disease (ESRD) on chronic dialysis therapy. While normal plasma Si concentrations are 0.15 ±.02 mg/L, all dialysis groups showed marked elevations in their plasma Si that correlated with the Si content of their respective dialysis fluids. The ultrafiltrability of plasma Si through Cuprophane membranes was 79 ± 2%. Hemodilysis (HD) patients drinking high Si containing well water showed significantly higher plasma Si levels than patients drinking lower Si municipal water. The use of dialysis fluid with elevated Si levels and the consumption of water containing high concentrations of Si are two important determinants of Si levels in a dialysis population. No overt effects of Si accumulation have been observed on the health status of the dialysis patients in this study.[8]

Elevated Si levels have been found in the serum of uremic patients, in the brain of patients with senile dementia and in neurological tangles of Alzheimer patients. The effect of Si on superoxide dismutase (SOD) was studied in vitro, since excessive superoxide production have been observed in renal failure, in inflammatory conditions and in the aging process. Si in concentrations similar to those found in serum of uremic patients inhibits SOD activity. The degree of inhibition was directly proportional to Si levels. Depression of SOD by Si is likely to result in a decrease in oxygen free radical destruction and thus an increase in excessive local availability of oxygen free radicals. The increased Si levels in brain, kidney, lung and Red Blood Corpuscles (RBC) which are especially sensitive to oxygenation damage may contribute to a variety of important clinical complications, by means of generating excess oxygen free radicals.[9]

Host factors influencing the absorption and excretion of Si are poorly understood, although previous murine and human studies have suggested that age, sex and oestrogen status may affect Si metabolism and thus its function. There was no difference in the absorption of Si into serum (overall profile, rate of Si appearance, peak concentration and time to peak) between the different adult groups. The rate of elimination of Si from serum did not significantly differ with age or sex, although serum concentration at 6 hours was higher in older adults and significantly correlated with age. There were, however, no significant differences in the excretion of Si into urine (a proxy for overall uptake) between the groups, averaging approximately 45%. Oestradiol levels did not correlate with any of the above measures of Si. Thus, overall, host age and sex did not appear to markedly influence Si absorption or excretion in human adults and no correlations were found with serum oestradiol status. The marginally higher baseline and 6 hours post-dose Si levels in older adults may reflect modestly impaired renal function and/or the loss of Si from connective tissues with ageing.[10]

Although Si is considered as an essential element, little is known about the basic effects and clinical significance of increased concentrations of the element in dialysis patients. In a multicentre study it was found that Si levels in HD patients were markedly increased. In these patients Si concentrations were significantly higher than those noted in subjects with normal renal function as well as in patients with Chronic Renal Failure (CRF) not yet in dialysis and patients treated by Continuous Ambulatory Peritoneal Dialysis (CAPD). Moreover it was noted that in both HD and CAPD patients mean Si levels differed from one centre to another.

Also, there was significant difference in serum Si levels among HD patients from different countries. The clinical relevance of increased serum Si levels is not yet known and as such deserves further investigation. In view of the controversy that exists on the element's assumed protective as well as toxic role in the development of some (aluminium-related) neurodegenerative diseases and its vital role in bone formation, monitoring of the Si levels in serum, tap water, and dialysis fluids might become important.[11]

SILICON AND CARDIO VASCULAR DISEASE

The association between crystalline silica exposure and risk of heart disease mortality remains less clear. Positive exposure-response trends were observed for cumulative silica exposure associated with mortality from total heart disease and Pulmonary Heart Disease (PHD). Low-level crystalline silica exposure was associated with increased mortality from heart disease, including PHD and Ischemic Heart DIsease (IHD), whereas high-level exposure mainly increased mortality from PHD. Current permissible exposure limits for crystalline silica in many countries may be insufficient to protect people from deaths due to heart disease.[12]

Silicon-enriched spirulina (SES) supplementation prevented vascular and endothelial functions assessed respectively by the contractile response to the agonist phenylephrine and the relaxation induced by acetylcholine. SES protects against metabolic imbalance, inflammation, oxidative stress, and vascular dysfunction induced by high fat diet, and could prevent the atherogenic processes since a synergistic effects were observed between spirulina and Si.[13]

SILICON AND BONE METABOLISM

Accumulating evidence over the last 30 years strongly suggest that dietary Si is beneficial to bone and connective tissue health and a study recently reported strong positive associations between dietary Si intake and Bone Mineral Density (BMD) in US and UK cohorts. The exact biological role(s) of Si in bone health is still not clear, although a number of possible mechanisms have been suggested, including the synthesis of collagen and/or its stabilization, and matrix mineralization.[14]

Physicians are aware of the benefits of calcium and vitamin D supplementation. However, additional nutritional components may also be important for bone health. There is a growing body of the scientific literature evidence which recognizes that Si plays an essential role in

bone formation and maintenance. Si improves bone matrix quality and facilitates bone mineralization. Increased intake of bioavailable Si has been associated with increased bone BMD. Si supplementation in animals and humans have been shown to increase BMD and improve bone strength. Si in the form of silica, or silicon dioxide (SiO_2), is a common food additive but has limited intestinal absorption. More attention to this important mineral by the academic community may lead to improved nutrition, dietary supplements and better understanding of the role of Si in the management of postmenopausal osteoporosis.[15]

Physicians are less likely to be aware that dietary insufficiencies of magnesium, Si, Vitamin K and Boron are also widely prevalent, and each of these essential nutrients is an important contributor to bone health. In addition, specific nutritional factors may improve calcium metabolism and bone formation and that nutritional supplements should attempt to provide ample, but not excessive, amounts of factors that are frequently insufficient in the typical American diet.[16]

Mean Femoral (FN) BMD was 2% lower in the lowest quartile compared to the top quartile of energy-adjusted Si intake. Energy-adjusted Si intake was associated with FN BMD for oestrogen-replete women only (late premenopauel women) and women on Hormone Replacement Therapy (HRT)). There was an interaction between oestrogen status and quartile of energy-adjusted Si intake on FN BMD, which was significant after adjustment for confounders, and stronger for bioavailable Si. Quartile of energy-adjusted dietary Si intake was negatively associated with free Deoxypyridinoline cross-links relative to creatinine (fDPD/Cr and Fpyd/Cr) and positively with N-terminal Propeptide of type 1 collagen(PINP). These observations suggests that oestrogen status is important for Si metabolism in bone health. Further works are required to elucidate this mechanism.[17]

Dietary Si correlated positively and significantly with BMD at all hip sites in men and pre menopaue women, but not in post menopause women, suggesting that increased Si intake is associated with increased cortical BMD in these populations. Si intake correlated positively with adjusted BMD at four hip sites in men and pre-menopause women, but not in post menopause women. No significant association was observed at the lumbar spine in any group. Categorical analysis by Si intake, or energy-adjusted Si intake, supported these findings, and showed large differences in BMD (up to 10%) between the highest (>40 mg Si/day) and lowest (<14 mg Si/day) quintiles of Si intake. A significant association at the lumbar spine in men was also observed. Further analyses indicated that some of the effects

seen for moderate consumption of alcoholic beverages on BMD might be attributed to Si intake. These findings suggest that higher dietary Si intake in men and younger women may have salutary effects on skeletal health, especially cortical bone health, that has not been previously recognized. Confirmation of these results observed must be followed up in future by longitudinal studies and by assessment of the influence of Si intake on bone markers in cohorts.[18]

Previous studies have reported that dietary Si intake was positively associated with bone health including BMD. Although the amount of Si intake was found to be high among trace elements in humans, how dietary Si affects bone formation at the cellular level is not well addressed. The increase of collogen type -I gene expression as a result of treatment with sodium metasilicate did not reach statistical significance. mRNA expression of insulin-like growth factor-I and receptor activator of NF-κB ligand was not significantly changed at any dose of sodium metasilicate. In light of these observations, Si was found to have a positive effect on bone metabolism by enhancing osteoblast mineralization activity.[19]

Convincing evidence shows that Si is a bioactive beneficial trace element continues to accumulate. The evidence, which has come from human, animal, and in vitro studies performed by several laboratories, indicate that Si in nutritional and supra nutritional amounts promotes bone and connective tissue health, may have a modulating effect on the immune or inflammatory response, and has been associated with mental health. A plausible mechanism of action for the beneficial effects of Si is the binding of hydroxyl groups of polyols such that it influences the formation and/or utilization of glycosaminoglycans, mucopolysaccharides, and collagen in connective tissue and bone. In addition, Si may affect the absorption, retention or action of other mineral elements (e.g., aluminum, copper, magnesium). Based on findings from both animal and human experiments, an intake of silicon of near 25 mg per day would be a reasonable suggestion for an adequate intake that would assure its nutritional benefits. Increased intakes of Si through consuming unrefined grains, certain vegetables, and beverages and cereals made from grains should be recognized as a reasonable dietary recommendation.[20]

Si a relatively unknown trace element in nutritional research, has been uniquely localized in active calcification sites in young bone. Si increases directly with calcium at relatively low calcium concentrations and falls below the detection limit at compositions approaching

hydroxyapatite. It is suggested that Si is associated with calcium in an early stage of calcification.[21]

Several studies revealed the requirement for Si in bone development, while bioactive silicate glasses simultaneously pioneered the current era of bioactive materials. Considerable research have subsequently focused on the chemistry and biological function of Si in bone, demonstrating that the element has at least two separate effects in the extracellular matrix: By interacting with glycosaminoglycans and proteoglycans during their synthesis, and by forming ionic substitutions in the crystal lattice structure of hydroxyapatite. In addition, the dissolution products of bioactive glass (predominantly silicic acids) have significant effects on the molecular biology of osteoblasts in vitro, regulating the expression of several genes including key osteoblastic markers, cell cycle regulators and extracellular matrix proteins. Researchers have sought to capitalize on these effects and have generated a diverse array of biomaterials, which include bioactive glasses, silicon-substituted hydroxyapatites and pure, porosities silicon, but all these materials share similarities in the mechanisms that result in their bioactivity.[22] Increasing evidences suggest that dietary Si intake, is positively correlated with bone homeostasis and regeneration, representing a potential and valid support for the prevention and improvement of bone diseases, like osteoporosis.[23]

SILICON AND IMPLANT

The blood Si levels in the implant tissue of patients were significantly higher than those of controls. However, there were no significant differences in the blood Si levels between these two groups of patients.[24] There was no significant correlation between past rupture of one or both implants, current rupture at the time of the blood draw, or the number of years with implants and Si levels. The observations suggest that serum Si levels are elevated in many women with silicone gel breast implants. However, the chemical species involved and kinetics of this elevation remain to be determined.[25]

The increase, in the last two decades, in the application of silicones (polysiloxanes) and inorganic Si compounds in medicine and the food industry have exposed the human body to extensive contacts with these substances. Most silicone breast implants contain a gel consisting of a cross linked silicone elastomer swollen by silicone oil (PDMS). Diffusion of PDMS through the silicone elastomer envelope and rupture of the envelope with release of the gel contents that occur clinically. The amount and distribution of silicone compounds in various tissues are key issues in the assessment of health problems connected with silicone

implants. To properly interpret the importance of these numbers for human health, a larger study of ”normal” levels of Si in human tissues should be undertaken and factors such as diet, water, race and geographical location should be considered.[26]

Si levels in breast milk, whole blood, cow's milk, and 26 brands of infant formulas were analysed. Comparing implanted women to controls, mean Si levels were not significantly different in breast milk (55.45 +/- 35 and 51.05 +/- 31 ng/mL, respectively) or in blood (79.29 +/- 87 and 103.76 +/- 112 ng/mL, respectively). Mean Si level measured in store-bought cow's milk was 708.94 ng/mL, and that for 26 brands of commercially available infant formula was 4402.5 ng/mL (ng/mL = parts per billion). Lactating women with silicone implants are similar to control women with respect to levels of Si in their breast milk and blood. Si levels are 10 times higher in cow's milk and even higher in infant formulas.[27]

CONCLUSIONS

This mini review on silicon in human health has brought out the following conclusions.

Si has wide applications for every aspect of human health. Its role in Kidney diseases, CVD, Bone health and Breast Implants have been studied to some extent. The sources, bioavailability, and its wide applications in various fields have also been investigated. However, the uses and health implications in the fields of Diabetes Mellitus, Liver, Infertility, endocrine and reproductive health needs to be done to realize its beneficial effects. More studies are required in this field to bring out the importance of Si and its merits and demerits in all possible human health and diseases and more research is required in the implications of Si in CVD. The contents of this review will certainly help future researchers to explore the uncovered fields in the metabolic and beneficial effects in many other health care benefits related to this trace element.

CONFLICT OF INTEREST -- None declared.

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