ISSN: 0975-833X

Available online at http://www.journalcra.com

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

International Journal of Current Research
Vol. 13, Issue, 11, pp.19728-19733, November, 2021

DOI: https://doi.org/10.24941/ijcr.42681.11.2021

RESEARCH ARTICLE

MICRONUTRIENTS: AN INDISPENSABLE PART OF PERIODONTAL HEALTH

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ARTICLE INFO

Article History:
Received 15th August, 2021
Received in revised form
29th September, 2021
Accepted 18th October, 2021
Published online 30th November, 2021

Keywords:

Micronutrients, Macronutrients,
Diet, Nutrition,
Periodontal Disease.

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ABSTRACT

Diet and nutrition are considered to play a cardinal role in maintaining overall health among individuals. Diet is the amount of food consumed by the individuals: whereas nutrition is the process of utilizing food for growth, metabolism and repair of tissues. Periodontal diseases are polymicrobial disease characterized by infiltration of leukocytes, loss of connective tissue, alveolar bone resorption, and formation of periodontal pockets. Periodontal disease is a chronic inflammatory disease, which leads to alteration of the micronutrient levels. Any imbalance of the micronutrient levels leads to increased susceptibility to oxidative damage of tissues. In order to sustain the periodontal tissues in both health and disease depends on the ample source of essential nutrients available to the host. Maintaining a balance of these trace minerals is essential to prevent progression of chronic conditions like periodontitis. Depletion or lack of availability of these nutrients gives rise to malnutrition at either the macro or micronutrient level, both of which are detrimental to periodontal health as well as to general health.

Citation: Dr. Ann Theresa Tomy, Dr. Saranyan, R., Dr. Manovijay, B., Dr. Meenalochani, T.B. and Dr. Vaishnavi, S. *"*Micronutrients: an indispensable part of periodontal health*", 2021. International Journal of Current Research, 13, (11), 19728-19733.*

INTRODUCTION

Diet and nutrition play a cardinal role in maintaining general and oral health among individuals. They have a collaborative relationship with health status. Diet refers to total amount of food consumed by the individuals: whereas nutrition is the process of utilizing food for growth, metabolism and repair of tissues (1). Based on the amount required by the body for normal metabolism, growth and physical well-being they are classified into-1. Macronutrients: namely carbohydrates, proteins and fat (2). Micronutrients: vitamins and minerals (2). There is a growing interest in the role of the micronutrients in optimising health, and in prevention or treatment of disease.

Periodontal diseases are microbial induced chronic inflammatory conditions characterized by infiltration of leukocytes, loss of connective tissue, alveolar bone resorption, and formation of periodontal pockets (3). In response to periodontal pathogens, leukocytes elaborate destructive oxidants, proteinases and other factors. Periodontal disease is a chronic inflammatory disease, which leads to alteration of the micronutrient levels such as zinc, selenium, iron and copper (4)

The imbalance of the micronutrient levels leads to increased susceptibility to oxidative damage of tissues (4).In order to sustain the periodontal tissues in both health and disease depends on the ample source of essential nutrients available to the host. And for optimum host response these micronutrients are a prerequisite.

Populations worldwide are prone to nutritional insufficiency due to lifestyle changes or poor nutritional intake (4). Maintaining a balance of these trace minerals is essential to prevent progression of chronic conditions like periodontitis. Depletion or lack of availability of these nutrients gives rise to malnutrition at either the macro or micronutrient level, both of which are detrimental to periodontal health as well as to general (5).

THE TRACE MINERAL IRON: It is the 4th most abundant element in our planet and an essential element for almost every living organism.It has also got an active role in various metabolic process. As it can form free radicals, concentration of iron in body tissues need to be tightly regulated because in excessive amounts, it can lead to tissue damage.

FAST FACTS ON IRON: Iron is a chemical element represented by Fe with an atomic number 26. This transition metal exists in several different oxidation states with Fe2+ (ferrous) and Fe3+ (ferric) being the most common. Total body iron content of a normal adult ranges from 4.3 and 2.3gms in men and women. The recommended daily allowance (RDA) varies between ages, but women who are pregnant requires the most. Iron promotes healthy pregnancy, increased energy and better athletic performance. Canned calms fortified cereals, white beans are best dietary source and others include liver, sardines, beef, lamb, egg, vegetables such as kale, broccoli, spinach and green peas, dried apricots. Excess much of iron can lead to risk of liver cancer and diabetes.

IRON AND ITS ROLE IN GENERAL HEALTH: Iron is an essential nutrient – indeed, the intimate relationship between iron and oxygen forms the basis of human life (7). Iron-containing haem serves as a cofactor for the protein's haemoglobin and myoglobin. Both have essential oxygen-carrying roles in our body. Red blood cell haemoglobin harbours about two-thirds of the total body iron content, helping to transport oxygen from the lungs to the rest of the body. Myoglobin provides short-term storage of oxygen in muscle to provide a supply at times of high demand. It's vital for both physical health and mental well-being, and performs three main functions:

- Transport of oxygen from the lungs to the rest of body
- To maintain a healthy immune system
- Aids in energy production

Dietary Fe is absorbed from the gut during depletion and transported in the form of ferritin. Its reduced absorption results in Fe deficiency anaemia where the haemoglobin levels are < 12 g/dL for adult non-pregnant women and < 13 g/dL for adult men. Furthermore, in Fe deficiency anaemia, decreased serum Fe and ferritin levels and increased total Fe binding capacity are seen. This should be distinguished from anaemia of chronic disease which is cytokine-mediated anaemia which is more prevalent in individuals with chronic inflammatory, infectious, or neoplastic disorders and characterized by hypoferremia with adequate reticuloendothelial Fe stores.

IRON IN PERIODONTAL DISEASE: Ample levels of Fe are an essential prerequisite for periodontal health and shift in either direction may be pernicious. Fe plays a significant role in innate and adaptive immune responses. Deficiency of Fe weakens the cell-mediated immunity by reducing lymphocyte count, interferon-γ and interleukin-2 levels and functions of natural killer cells. Disruption of delayed type of hypersensitivity response mediated through CD4+ lymphocytes is also observed. It also results in reduced immunoglobulin E (IgE) production, high CD4+ to CD8+ T cell ratios, low numbers of CD28+ cells and impaired CD8+ T-cell function (9). Fe plays an important role in oxidative burst, i.e., the release of reactive oxygen species (ROS) from macrophages and neutrophils (10). A shift in the levels of Fe may cause oxidative stress leading to periodontal destruction (4). And is mainly related to the conversion of hydrogen peroxide to ROS through Fenton reactions catalysed by free Fe. Both chronic periodontitis and iron deficiency anaemia induce oxidative stress in the body and cause an imbalance between reactive oxygen species and antioxidants, such as superoxide dismutase (11) Chakraborty et al, reported that chronic periodontitis as well as iron deficiency anaemia in patients with and without periodontitis are associated with decreased salivary and serum superoxide dismutase levels compared to healthy controls. A significant, negative correlation was observed between serum superoxide dismutase levels and all periodontal parameters. Patients with iron deficiency anaemia and chronic periodontitis exhibited a higher incidence of bleeding on probing, a higher percentage of sites with clinical attachment loss of ≥6 mm, as well as deeper periodontal pocket depths, than patients with chronic periodontitis only in their study.

Patients with chronic periodontitis have a lower number of erythrocytes and a lower haemoglobin level than healthy controls. In a prospective study on a rural Japanese population, Yamamotto et al confirmed that, after adjusting for age, the progression of periodontal disease is associated with a decrease in erythrocyte counts. It was proposed that chronic periodontitis can lead to anaemia of chronic disease, which may be explained by a depressed erythropoiesis resulting from the systemic effect of the proinflammatory cytokines as a response to periodontal pathogens and their products. The role of Fe in periodontal ligament and alveolar bone homeostasis and function was recently studied in an animal model(4).The PDL cells have the ability to regulate Fe uptake by expressing the light and heavy chain subunits of heteromeric ferritin (4) which in turn can affect the cyto-differentiation of these cells into osteoblasts and mineralization, thereby bone density. Hence Fe is essential for immunological homeostasis. And both elevated and reduced levels are detrimental to the host immune responses, as well as susceptibility to infections. So, it is important to control and regulate its levels to guarantee the protective responses to health.

THE TRACE MINERAL COPPER: Copper is an essential trace mineral necessary for survival of life. Copper's essentiality was first discovered in 1928, when it was demonstrated that rats fed a copper-deficient milk diet were unable to produce sufficient red blood cells (12) .The anaemia was corrected by the addition of copper-containing ash from vegetable or animal sources. As an essential trace element, daily dietary requirements for copper have been recommended by a number of governmental health agencies around the world.

FAST FACTS ON COPPER

Copper is a chemical element represented by the symbol Cu with an atomic number 29 .The adult body contains between 1.4 and 2.1 mg of copper per kilogram of body weight(8) .

The Recommended daily allowance for Cu is 900 µg. The richest dietary copper sources include shellfish, seeds and nuts, organ meats, wheat-bran cereals, whole-grain products, and chocolate (1,2). The absorption of copper is strongly influenced by the amount of copper in the diet; bioavailability ranges from 75% of dietary copper when the diet contains only 400 mcg/day to 12% when the diet contains 7.5 mg/day (3). Tap water and other beverages can also be sources of copper, although the amount of copper in these liquids varies by source (ranging from 0.0005 mg/L to 1 mg/L) (2,11). Copper deficiency is uncommon in humans (2). Based on studies in animals and humans, the effects of copper deficiency include anaemia, hypopigmentation, hypercholesterolemia, connective tissue disorders, osteoporosis and other bone defects, abnormal lipid metabolism, ataxia, and increased risk of infection.

COPPER AND ITS ROLE IN GENERAL HEALTH

It is present in almost every tissue of the body and is stored chiefly in the liver along with the brain, heart, kidney, and muscles. It plays a role in making red blood cells and maintaining nerve cells. Cu is essential for immunity and combating the oxidative stress induced by reactive oxygen and nitrogen species. It acts as a co-enzyme for cytochrome-C and superoxide dismutase and is involved in electron transport of proteins. Required in association with Fe for the formation of hemoglobin and is stored bound to ceruloplasmin, a Cu dependent ferroxidase. Ceruloplasmin helps in oxidising Fe so that ferritin is utilized. Therefore, its deficiency may cause anemia. Cu plays an important role in cytochrome oxidase functions at the terminal end of the mitochondrial electron transport chain. The loss of this activity can contribute to the characteristic swelling and distortion of mitochondria, which can be observed in Cu deficiency, particularly in metabolically active pancreatic acinar cells, enterocytes, and hepatocytes (58). Abnormal metabolism of Cu can affect the function of superoxide dismutase and results in decreased protection of cells from superoxide radical. Hyperglycemia and hyperinsulinemia increase the production of free radicals and decrease the efficiency of antioxidant defense systems, which may lead to the complications of diabetes.

COPPER IN PERIODONTAL DISEASE

Deficiency of copper can lead to negative impact on functioning of neutrophils, macrophages, T cells and natural killer cells. There is an excessive production of proinflammatory cytokines, such as tumor necrosis factor-α, matrix metalloproteinase-2 and -9 which degrade the collagen and extracellular matrix components in periodontal ligament impaired production of interleukin-2. In a study conducted by Thomas et al it was concluded that elevation of serum Cu level is observed in periodontitis patients causing certain alterations in collagen metabolism (13). Cu is essential for proper connective tissue development and the elevation in serum Cu may reflect the changes in periodontal collagen metabolism (4). Another study by Sundaram et al.(14)In their study demonstrated the levels of Cu in diabetes and non-diabetes patients with chronic periodontitis; Cu levels were elevated at baseline and were improved significantly 3months following nonsurgical periodontal therapy, even in those participants with uncontrolled type 2 diabetes mellitus. Manea and Nechifor(15) in their study has shown that there exists a connection between salivary copper levels and periodontitis. As Cu serves as a cofactor for metalloenzyme like superoxide dismutase, an essential antioxidant for chronic periodontitis, optimal levels of Cu are essential for preventing exacerbation of inflammatory pathways(4).

THE TRACE MINERAL SELENIUM: Another trace mineral needed by human is selenium due to its potent anti-inflammatory, antioxidant and antiviral properties. Selenium was discovered in 1817 Jöns Jacob Berzelius. Selenium is listed as an active ingredient in many multivitamins and other dietary supplements, as well as in infant formula, and is a component of the antioxidant enzymes glutathione peroxidase and thioredoxin reductase also in three deiodinase enzymes.

FAST FACTS ON SELENIUM: Selenium is a chemical element with the symbol **Se** and atomic number 34.The recommended daily allowance for Se is 55 µg for adult men and adult women.17. Dietary selenium is attained through a wide variety of food sources, including cereals and other grains, soybeans, vegetables, seafood, meats, eggs, dairy products, yeast, and nuts (16). Different studies have revealed wheat and meats as the most important sources, as selenium tends to be present in relatively high concentrations in such foods and, compared with selenium salts, selenium in these foods is highly bioavailable (17). Selenium is covalently bound into multiple compounds, whereby the chemical form of selenium partially determines its metabolism. The major form of selenium ingested by humans is the amino acid selenomethionine (18). Inorganic salts of selenium (eg, selenite, selenate), as well as selenomethionine, can be converted to selenide. Selenide has 2 potential metabolic pathways, one of which is sequential methylation and excretion in the urine. The other pathway results in the formation of selenoproteins, which are proteins with enzymatic activity that incorporate selenium. Selenium deficiency may be related to poor dietary intake, presence of chronic diseases and ingestion of drugs that reduce its absorption and proper utilization. Some studies pointed out that even alcohol intake may result in poor concentrations of Se.

SELENIUM AND ITS ROLE IN GENERAL HEALTH: The anti-oxidant activity of selenium adds to the beneficial effect of this mineral. They are also involved in the activation, proliferation, and differentiation of cells that drive innate and adaptive immune responses. Dietary selenium and selenoproteins are also involved in immunoregulation, considered to be crucial for preventing excessive responses that may lead to autoimmunity or chronic inflammation (18). Property of selenium and selenoproteins to take part in cellular maintenance, protein folding, and the oxidative stress response can lead to multifactorial diseases. Also, alteration of selenoprotein synthesis or activity has been linked to the development of chronic diseases, such as cancer. Although epidemiological studies indicate that low selenium intake is linked to increased risk for various chronic diseases, supplementation trials have revealed confusing outcomes, suggesting that additional nutrigenetic factors could affect the relationship between selenium and health (19).

SELENIUM IN PERIODONTAL DISEASE: In vitro and animal studies showed that addition of Se to α-tocopherol accelerated the proliferation rate and wound healing process. This was related to the increased synthesis of basic fibroblastic growth factor and type I collagen from both gingival and periodontal ligament fibroblasts in the presence of Se (20,21).

Thomas et al. evaluated the concentrations of glutathione, catalase, and Se in the serum of middle-aged patients with type 2 diabetes mellitus and healthy individuals, with and without periodontal disease(22).The levels of glutathione, catalase, and Se were found to be significantly lower in patients with diabetes and periodontitis compared with healthy controls. Se levels in healthy individuals with periodontitis were also decreased; however, this didnot reach significance. A co-morbid impact of periodontitis with diabetes upon systemic micronutrient status was seen, probably because of oxidative stress (23). Hence, selenium is considered to be a protective trace mineral for the periodontium and its inclusion in the diet may be vital in "dietary regulation of inflammatory cascade, "thereby controlling destructive periodontal disease.

THE TRACE MINERAL ZINC: Zinc is considered to be yet another trace mineral which is required by our body to maintain a healthy condition. It has got biological functions like growth, development, wound healing, cell proliferation, differentiation, gene expression, integrity and stabilization of bio membranes and the cytoskeleton, antioxidant functions, immune competence, and metabolism. German chemist Andreas Sigismund Marggraf is credited with discovering pure metallic zinc in 1746.Of the trace minerals, this element is second only to iron in its concentration in the body.

FAST FACTS ON ZINC

Zinc is a chemical element with the symbol Zn and atomic number 30. The recommended daily intake (RDI) is 11 mg for adult men and 8 mg for adult women. Many animal and plant foods are naturally rich in zinc, making it easy for most people to consume adequate amounts. In biological systems, zinc exists as Zn2+ and is present in all tissues and fluids of the body. There is 2–4 g of Zn distributed throughout the human body(31). Zn is stored in prostate, parts of the eye, brain, muscle, bones, kidney, and liver. Foods enriched in zinc include: Shellfish, Meat, Poultry, Legumes, Nuts and seeds, Dairy products, Eggs, Whole grains, Certain vegetables. Chronic ingestion from zinc supplements in excess of the recommended daily allowance has been associated with the suppression of immune responses, decrease in high-density-lipoprotein cholesterol reduced copper absorption, and impaired copper status (24).

Excess zinc also interferes with the action of lysyl oxidase, an enzyme that catalyzes collagen crosslinking, and hence of importance for the structural integrity of connective tissues and for wound healing (26,25). This micronutrient participates both in the synthesis and actions of the hormones, which are intimately linked to bone metabolism(30).In blood plasma, Zn is bounded and transported by albumin (60%) and transferrin (10%) (31). An antagonistic relationship between zinc and iron has been reported (27). Daily intake of iron at levels such as those found in some supplements could decrease zinc absorption and vice versa. Mechanistically, Zn is involved in the processes of genetic stability and gene expression in a variety of ways including the structure of chromatin, the replication of DNA and transcription of RNA through the activity of transcription factors and RNA and DNA polymerases, as well as playing a role in DNA repair and programmed cell death (Falchuk 1998).

ZINC AND ITS ROLE IN GENERAL HEALTH

Zinc has got a crucial role in immune responses. It can interact specifically with components of the immune system. Zinc is relevant for immunocompetence, because it bounds to enzymes, proteins and peptides with different binding affinity (Mocchegiani et al. 2000) (28). Zinc is transported to cells bound to proteins, predominantly albumin, a2-macroglobulin and transferrin, but only free Zn ions seem to be biologically active (Vallee and Falchuk 1993). In addition, zinc is essential for intracellular binding of tyrosinekinase to the T-cell receptors, CD4 and CD8α, whichare required for T-lymphocyte development and activation(29).Zn is considered to be an integral component of antioxidant enzymes and its altered levels can lead to oxidative stress.

ZINC IN PERIODONTAL DISEASE: Optimal levels of Zn are imperative for growth and development of periodontal tissues (4). The deficiency leads to reduced protection of sulpha-hydryl groups and increased production of ROS. At increased level it may act as a pro-oxidant by eliciting a decline in erythrocyte Cu-Zn superoxide dismutase. This enzyme has been localized in the human periodontal ligament where it prevents free radical induced damage (32,33). To maintain health an optimum level is considered to be a prerequisite. Various animal studies have concluded that dietary deficiency of Zn leads to poorer periodontal health. The thickness and keratinization of oral mucosa becomes more susceptible to infections. Zn deficiency has also been shown to reduce osteoblastic activity, collagen and proteoglycan synthesis as well as alkaline phosphatase activity(4). In Sweden a study conducted by Frithiof et al, analyzed Serum zinc levels and the severity of periodontal disease in patients undergoing periodontal treatment, Patients with decreased Zn levels showed increased alveolar bone resorption (34). This could be related to altered bone collagen metabolism with a significant reduction in collagen synthesis and turn over as well as reduced alkaline phosphatase activity (34).

Thomas et al, compared serum zinc levels in a group of patients with diabetes and periodontitis, with those in a group of patients with periodontitis but not diabetes, and with those in a group of systemically and periodontally healthy control subjects, all from South-West India (35,36). The zinc levels were significantly lower in periodontitis patients, with and without diabetes, than in healthy individuals (36). Sundaram et al examined the effect of nonsurgical periodontal therapy on serum zinc concentration in patients, from India, with type 2 diabetes mellitus and chronic periodontitis. Forty participants were systemically healthy and assigned to group I (37). The remaining subjects had a history of diabetes for longer than 5 years and were equally divided into group II (well-controlled type 2 diabetes mellitus) or group III (uncontrolled type 2 diabetes mellitus and hemoglobinA1c > 8%) (38). Three months after treatment, the serum concentration of zinc increased compared with baseline in all 3 groups. Significantly elevated zinc levels were also detected in both groups of periodontitis patients with both controlled and uncontrolled diabetes (38).

CONCLUSION

Oral health may be compromised by a number of aging factors such as, lack of appetite and masticatory ability, altered taste, loss of teeth, oral prosthesis and other gastrointestinal conditions Considering the role of nutrition for oral and

periodontal health, nutritional advice can be very helpful for the prevention and management of periodontal diseases. Regular and timely dietary consultation during dental practice can improve the quality of life, hence added advantage to the elderly.In case of deficiency of any micronutrients, dietary sources or nutritional supplements must be considered.

Conflicts of interest: nil

Source of funding: nil

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