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Review Article

Antioxidant and Bone; Protect Your Future: A Brief Review

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Abstract

The global campaign of osteoporosis has been organized by the International Osteoporosis Foundation (IOF) and them introducing World Osteoporosis Day (WOD) in 1997. The day is celebrated on October 20th each year and aimed to improve the awareness of the population about disease prevention. We present some aspects of bone health and the prevention of osteoporosis related to the use of vitamins. The presenting mini-review covers a variety of sources including PubMed, Embase, Scopus, and directory of open access journals (DOAJ) from 10 years ago (Oct 2009 to Oct 2019) for recent developments in the prevention of bone loss. The search was performed by using combinations of the following keywords and or their equivalents; osteoporosis, bones health, bone loss, and vitamin to find related articles about the prevention of osteoporosis by nutritional factors. The factors affecting bone are various and could begin from fetal periods to the end of life. Some of them are not changeable including age, and genetic; however, it is possible to modify some others such as poor nutrition and vitamin deficiency. Beyond vitamin D deficiency, consumption of other vitamins also is beneficial to maintain bone health. By considering the nutritional factors especially vitamins that affect bones, it is possible to have stronger bones to enjoy life in the elderly and protect your future.

Keywords: Osteoporosis; Bones health; Bone loss; Vitamin

Introduction

Modifiable risk factors of osteoporosis

Before birth, the skeleton has been formed, to support humans throughout life, and even long after death; thus, this necessary organ should be taken care of by everyone (1). The bone mass is the consequence of the peak bone mineral density achieved in young adulthood and the subsequent rate of bone loss in later life. As a dynamic tissue, bone is always renewed during the entire period of life through the process of bone remodeling, involving the removal of old bone by osteoclasts and the creation of new bone by osteoblasts (2). After the age of 35 yr, the total amount of bones is going to decrease (2). The gradual loss of bone which may occur over the years causes fragility of bone and results in osteoporosis. Beyond genetic factors, which are major determinants of peak bone mass (3), other modifiable factors including vitamins could affect rates of change of bone mass in adulthood (3,4) and determined the development of osteoporosis. The modifiable factors affecting osteoporosis are various including, cigarette smoking, alcohol intake, sex hormone deficiency, medications, nutritional factors such as inadequate calcium, and excessive oxidative stress (5, 6).

Oxidative stress and bone loss

Metabolic activities of living cells such as activation of various mitochondrial and cytoplasmic enzymes cells produce oxidation reactions and free radicals including reactive oxygen species (ROS) (6). A controlled increase of ROS level may have an important role in the transmission of intracellular signaling which regulates many fundamental cellular processes such as proliferation, differentiation, and repair processes (5, 6). However, ROS are also harmful products that can accumulate and cause structural damage to the cell. The increased level of ROS in bone cells causes damage and apoptosis genomic DNA of osteoblasts and osteocytes (7). Thus, the increase of ROS has been linked to an increase in osteoclastogenesis and osteoclast activity. Furthermore, excess amounts of these radicals also cause a variety of health problems including tissue inflammation, premature aging, and osteoporosis (8). In addition, lipid peroxidation-dependent lipoxygenase activated by ROS plays an important role in bone loss associated with aging (9). Equilibrium in the physiological intracellular redox state is maintained by various mechanisms that balance between the production of ROS and the level of antioxidants (5). When there is an imbalance between free radical productions and neutralizing antioxidant capacity oxidative stress (OS) occurs (10).

Oxidative stress (production of ROS in excess) by itself and indirectly by influencing the release of inflammatory cytokines such as tumor necrosis factor and interleukins could have an important role in bone loss and be involved in the pathogenesis of osteoporosis in the postmenopausal period and elderly (7,11). Oxidative stress also might have an important effect on the pathophysiology of men's osteoporosis (12). Therefore, use of the antioxidants could be helpful in the prevention of bone loss.

Antioxidant system and bone health

Both physiological events, such as aging, hormonal changes, and pathological events related to the production of inflammatory cytokines, toxins, and drug therapies affect the production of ROS (13, 14). ROS, as the major determinant of OS, induces the apoptosis of osteoblasts, osteocytes, and ontogenesis, which leads to increased bone remodeling and bone loss (15). ROS are neutralized in the body by the antioxidant system to prevent cellular damage (15,16). There is evidence that changes in antioxidant systems or levels of OS seem to be involved in the pathogenesis of bone loss (15,17).

Physiologic increase in the amount of antioxidants occurs in aging, but this amount is insufficient for neutralizing OS (15,17). Total antioxidant capacity among elderly osteoporotic women was lower than the normal age-matched population (18).

Under physiological conditions, several factors regulate bone remodeling by affecting osteoclast and osteoblast activity (7). Among these the most important are: the ligand of receptor activator of NF-kB (RANKL) and osteoprotegerin (OPG) that, their expression is sensitive to OS (15). Increased oxidative stress, which induces RANKL activates the differentiation and activity of osteoclasts with subsequent bone resorption. While OPG, as a soluble receptor capable of binding and blocking RANKL, results in inhibition of osteoclast activity and contributes to the differentiation of osteoblasts and mineralization (15,16, 19). Healthy bone is tightly regulated and maintained by the balance between these factors. Oxidative stress alters the bone remodeling process causing an unbalance between osteoclast and osteoblast activity, thus favoring bone resorption (15, 18).

Inadequacy of Antioxidant system and bone loss

Antioxidants are endogenous or exogenous molecules that neutralizing oxidative stress and its consequences. In inflammatory status or physiologic process, the of free radicals causes oxidative stress that neutralizes by an anti-oxidative mechanism and maintains redox conditions in the cell. Antioxidant deficiencies can develop as a result of excessive utilization or decreased antioxidant intake (20). The antioxidant

system comprises of agents such as vitamins E and C, glutathione peroxidase and superoxide dismutase (21). This system reduces oxidative stress by neutralizing or inhibiting the formation of free radicals and protects body systems, thus increase healthy longevity.

A systemic inflammatory status may develop in tissue by the imbalance between released radicals, and amounts of antioxidants (21). This imbalance is involved in the pathogenesis of osteoporosis and has an important role in bone loss of postmenopausal women (15, 17) and the elderly (19).

Antioxidants are thought to play a crucial role in postmenopausal bone loss. Estrogen deficiency by lowering thiol antioxidants in osteoclasts directly sensitizes these cells and by enhancing the expression of cytokines promotes osteoclastic bone resorption (20,21). Therefore, combinations of antioxidants may have long-term benefits for treating bone mineral loss in postmenopausal women.

Thus, augmentation of the antioxidant system to combat oxidative stress could prevent bone loss and antioxidant therapy could potentially reverse the adverse consequences of oxidative stress on the bone, especially among high-risk groups (20, 22-25). Now it is a question: how to boost the antioxidant system in adults and protect bones?

One of the practical approaches to augment the antioxidant system is to pay attention to the diet of the patient on the risk of osteoporosis. A diet containing a rich amount of vitamins or the use of supplements contain antioxidants could be reasonable for high-risk groups. Antioxidant supplementation that contains vitamins and minerals has become an increasingly popular practice to maintain optimal body function.

Supplementation of antioxidants for prevention of osteoporosis

As recent studies have indicated a correlation between the level of oxidative stress and osteoporosis (11, 12), therefore natural antioxidant should beneficial for the prevention of bone loss. Vitamins E and C are natural antioxidant vitamins, which prevent bone loss (5) by controlling excessive free radicals formation and subsequent effects in the body.

Vitamin E is a strong antioxidant, and by scavenging, ROS could to protect bones from oxidative damage. There is evidence for prevention of calcium loss, increases trabecular bone mass, and maintaining bone matrix by stimulates trabecular bone formation (15, 26-29). Researchers showed supplemental vitamin E can prevent the rise of serum IL-1 (30-32) and have protective effects in bone loss induced by sex hormones deficiency or nicotine-exposed rats, but not in human beings. Vitamin E deficiency also impaired vitamin D metabolism and calcium absorption.

Although there are limited studies, there is evidence for the positive effects of vitamin E on bone health and indicate some anti-osteoporotic benefits by the use of vitamin E. In a large cohort of older women, the relationship between vitamin E, and bone health was studied. There was a positive association between serum α-tocopherol and bone density at the femoral neck.

The most abundant and active form of vitamin E in human tissues and serum is α-tocopherol, which commercially is available as a supplement (18). This active form of vitamin E is naturally found in cereal grains, rice bran, almonds, green vegetables, and palm oil (16,17). The daily recommendation for vitamin E is 15 milligrams (mg), but many supplements come in 200-400 mg doses, and the maximal safe dose for vitamin E is 800 to 1000 mg per day.

Vitamin C is a water-soluble vitamin capable of being an antioxidant and prevent the effects of free radicals in the body. Vitamin C mediates differentiation and apoptosis of osteoclast, but vitamin C deficiency can decrease the number and differentiation of osteoblast (21-24). These findings in concordance with, effects of vitamin C supplementation on an increase in the number of osteoblasts suggest its effect on the accentuation of osteoblastogenesis and bone formation (30). Otherwise, vitamin C also has an important role in collagen biosynthesis and the quality of collagen fibers (29-32). Thus, vitamin C deficiency

promotes bone loss decreases bone matrix stability, and causes weak bones.

A prospective study in US elderly men and women showed a risk reduction of 44% in the incidence of hip fracture by regular intake of vitamin C supplements (33). Another Nutritional Survey in Korean adults showed that a higher intake of vitamin C was, associated with a lower risk of osteoporosis among those with low physical activity (34). A case-control study of osteoporotic patients suggests that prolonged vitamin C supplementation (500 mg daily) affects osteoclasts activity and may be beneficial in the treatment of osteoporosis (35).

Vegetables and fruits are the best sources of vitamin C and provide daily recommended intake (100-200 mg). For older adults who suffer chronic diseases, daily intake of at least 400 mg vitamin C prevents oxidative damage and clinical improvement (36).

Carotenoids are a group of lipid-soluble plant pigments, including β-carotene, α-carotene, lycopene, β-cryptoxanthin, and lutein (37). These substances are found in some vegetables (spinach, carrot) and fruits in red color. One of these carotenoids, which is a potent antioxidant, is lycopene. Tomatoes provide over 80% of the lycopene in the diet and their supplementation decreases oxidative stress and exhibits beneficial effects on bone health (38), but the mechanisms through which it alters bone metabolism remain unclear.

An experimental study on ovariectomized rat showed that lycopene prevents bone loss and improve bone strength, mainly in trabecular bones (39). In a human study in postmenopausal women also supplementation with lycopene had a beneficial effect in reducing oxidative stress and the bone resorption marker.

Polyphenols are antioxidants naturally found in fruits, vegetables, and tea (40). A review of the current literature suggests that habitual consumption of diets rich in polyphenols could be protected against cancers, type 2 diabetes, cardiovascular diseases, and osteoporosis (41-44). There are a few clinical studies on polyphenols and most of the research has emerged from in vitro or animal studies. A review by Cory and colleagues revealed an anabolic role for polyphenols on bone remodeling (45), while another study suggests the protective effects of polyphenol consumption for bone loss in postmenopausal women (46).

Conclusion

The aging of the population would increase the prevalence of osteoporotic fragility fracture and caused a socioeconomic challenge. Bone loss in the elderly is caused by different factors, among which oxidative stress is an important one. Therefore, neutralizing excessive oxidative stress with aging or in postmenopausal women could be a useful preventive measure for osteoporosis. A neutral antioxidant such as vitamin supplements with balancing effects of oxidative stress on aging bone and bone remodeling pathways could have beneficial effects for involution bone loss. For better determination and true effect of antioxidants and appropriate dosing for prevention of osteoporosis further research is needed.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

Conflicts of interest

The authors declare no conflict of interest.

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