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A review on the role of macro and micro nutrients in bone health

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ABSTRACT

Osteoporosis is a major public health problem, affecting many individuals. The aging population will require problem related prevention, education, and treatment to maintain bone density and reduce the bone fractures and falls. Inadequate intake of nutrients increases the risk for bone loss and subsequent osteoporosis. Protein, calcium and vitamin D are vital nutrients for optimal bone health. Adequate calcium is essential for bone maintenance. There are several other vitamin and mineral needed for metabolic processes related to good bone health, including manganese, copper, iron, zinc, vitamin A, vitamin K, vitamin C and the B vitamins. Related macro- and micronutrients play an important role in bone mass integrity and quality. Adequate nutrition for older adults needs to be encouraged to promote and maintain bone health.

Keywords: Calcium, Fractures, Osteoporosis, Vitamin D, Bone mass density

INTRODUCTION

The adult human consists of 213 bones which excludes the sesamoid bones.[1] Appendicular skeleton consist of 126 bones whereas axial skeleton consists of 74 bones and auditory ossicles consists of six bones. The bone undergoes remodeling during life which helps it to adapt to it to bio-mechanical forces and removes the old, damaged bone and replace it with new bone. Diet plays a key role in growth and development of body and it is primarily comprised of macronutrients and micronutrients. The macronutrients are proteins, carbohydrates, fats and dietary fibers whereas micronutrients are various vitamins and minerals. Osteoporosis, characterized by reduced bone mass and there is disruption of bone architecture that results in increased risk of fractures, is a major problem worldwide. Life expectancy is increasing nowadays and at present it is ~67 years in India and it is expected to increase to 71 years by 2025 and to 2050.[2] At present the Indian population is older than 50 years; however, it is likely to increase upto 34% by 2050.[3]

MACRONUTRIENTS

Protein

Protein is an essential element and it has a role in production of organic matrix of bone for synthesis of collagen. There are risk factors associated with high protein intake such as osteoporosis.[4,5] Dietary protein plays an important role in skeletal health as it affects bone in several ways: (1) large component of the organic structural matrix of bone, (2) it regulates serum concentrations of insulin-like growth factor (IGF)-1, and (3) it can affect calcium metabolism (calcium excretion and absorption).[6-8] Research studies suggest high-protein diet is detrimental to skeletal health, as hypercalciuria occurred in a majority of studies after individuals

consumed high dietary protein.[9,10] Increased absorption, and not skeletal mineral dissolution, was the main source of the elevated calcium excretion. Researchers have suggested increased protein intake increased Insulin like growth factors (IGF-1).[11] However high protein and calcium diets have known to play a beneficial role in inducing favorable changes in bone in children, postmenopausal women and elderly.[12-14] The recommended dietary allowance of protein was found to be 0.8gm/kg body weight.

Carbohydrate

Carbohydrates can augment skeletal growth by increasing calcium absorption and neutralizing metabolic acid loads with substantial potassium content.[15] Variety of fruits and vegetables contain nondigestible carbohydrates (inulin-type fructans) which cannot be digested by mammalian enzymes.[16] Not being broken down in the small intestine, travel to the colon where they are fermented to produce organic acids, lowering the luminal pH of the large intestine. The reduced pH alters calcium speciation which increases calcium solubility in the lumen which enables calcium bioavailability and enhances passive transport into the body.[17,18]

MICRONUTRIENTS

Minerals

Calcium is the most abundant and essential mineral which makes up about 1.5 to 2% body weight and 39% of total body minerals. Calcium as hydroxyapetite crystals is deposited in bone matrix and is obtained from cheese, milk, and yogurt, but dairy products are not the only source of dietary calcium. Recommended dietary allowances of 600 mg/day by Indian council of Medical Research is suggested for adult women.[19] In a randomized control trial it was found that 52 out of 54 controlled intervention trials the calcium on bone throughout life showed an increasing calcium intake that led to increased calcium balance, increased bone gain during growth and reduced bone loss in later years including reduced fracture incidence. Evidence suggests calcium supplementation reduces the rate of hip fracture by 25–70%, vertebral fractures by 23% and nonvertebral fractures by 14%.[20,21] Recommended calcium intake of 1200 mg/d in young adults and 1500 mg/d in postmenopausal women (whose not on hormone replacement therapy).[22]

Phosphorous is also an essential mineral that is required for mineralization of skeletal structure. About 80% is present in the skeleton and teeth in the form of calcium phosphate crystals. Phosphates combine with calcium ions to form hydroxyapetite crystals that are the major inorganic molecule that is present in bone. Nutritional recommendations of phosphorous is 1250 mg/d for adolescents, 700 mg/d for adults, and 580 mg/d for 51 yrs and older.[23] Diet that is high in phosphorus and low in calcium causes increased parathyroid hormone (PTH) levels in young adults after 4 weeks.[24] The ratio of phosphorus to calcium intake is essential in bone health rather than the absolute intake of phosphorus.[25,26] A ratio of 2:1 of calcium to phosphorous is recommended for healthy bone production.[27]

The adult human body has 60% of magnesium, about which half of the quantity is present in the bones in combination with phosphate and carbonate and one fifth of total magnesium is present in soft tissues. Deficiency of this mineral could affect bone growth, alter calcium metabolism, osteoblastic and osteoclastic activity, osteopenia, bone fragility.[28] The clinical features associated with magnesium deficiency are irritability, tetany, hyper-reflexia and occasionally hyporeflexia. Daily requirement is 340 mg/day for adults.[29]

Flourine is highly reactive, it is never found in elemental gaseous form, formed only in combined form. 96% fluoride in body is found in teeth and bone. It is important for normal mineralization of bones and formation of dental enamel. In most parts of India fluoride content is about 0.5 mg/l but in endemic flourosis area the fluoride content can be as high as 3 to 12 mg/litre. The recommended levels are 0.5 to 0.8 mg/litre.[30,31] Studies have shown that fluoridated water at 1 ppm reduces the risk of overall fractures, however flouride levels >4.32 ppm increases the risk of fractures.[32,33]

Potassium occurs widely in foodstuff, so there is likelihood of its deficiency. It is present in fruits and vegetables that provide an alkaline environment reducing the demand for skeletal salts to balance the endogenous acid generated from acid producing foods. The daily potassium requirement 3500 mg/day for 1–3 years, 3800 mg/day for 4–8 years, 4500 mg/day for 9–18 years, and 4700 mg/day for 19 years and older.[34]

Zinc is the component of many enzymes and is needed for osteoblastic activity, collagen synthesis, and alkaline phosphatase activity. Osteoporosis is related to low serum zinc levels and its deficiency has reported to result in growth failure and sexual infantilism.[35] The Recommended Dietary Allowance is 8 mg/d in women and11 mg/d in men and its level increases to 15 mg/d in postmenopausal women.[36]

Iron is of great importance in human nutrition. It is in two forms haem-iron and non-haem iron. Heam iron is rich in liver, meat, fish and poultry whereas non haem iron is present foods like cereals, legumes, green leafy vegetables and dried fruits. Haem iron is well absorbed, helps in absorption of non-haem iron. Iron is necessary for many functions in the body in the formation of hemoglobin, regulation of body temperature, muscle activity, is a cofactor in enzymes that are involved in collagen bone matrix synthesis and 25-hydroxycholcalciferol hydroxylase converts vitamin D to an active form that affects calcium absorption.

Copper in human body contributes to skeletal mineralization, bone formation and the maintaining integrity of connective tissues. Enzymes such as lysyl hydroxylase play an essential role in cross-linking of collagen fibrils. The RDA of copper is 0.9 mg/d and its daily intake should be less than 10 mg/d.[37] It is readily available in foods such as meat, nuts, seafood, nuts and grains.

Like copper and zinc, manganese is also required in trace as it is needed for synthesis of mucopolysaccharides for the formation of bone matrix. The RDA is 1.8 mg/d for women and 2.3 mg/d for men.[38] Sources are cereals, nuts, pineapples, beans, cinnamon, tea and dark chocolates. Study by Strause et al suggested supplementation of manganese with calcium, zinc and copper compared to calcium alone showed a gain in bone in postmenopausal women.[39]

Vitamins

Vitamin A contributes to various body functions as it supports the skeletal growth, essential for bone remodeling. It is both a preformed vitamin (retinol) and a provitamin (beta carotene), some of it is converted to retinol in the intestinal mucosa.[40] Food rich in carotene is eggs, liver, cheese whole milk and butter, the richest source of retinol is fish liver oil. There are morphological changes in bone due to its deficiency whereas its excess is associated with higher risk of fracture and low BMD.[41] RDA is 2333 IU in women and 3000 IU in men.[42]

Vitamin C is an antioxidant plays an important role in collagen formation, is a cofactor in the hydroxylation of proline and lysine which is required in crosslinking of collagen fibrils in bone. The RDA is 75 mg/d in women and 90 mg/d in men.[43] Sources are fresh fruits and green leafy vegetables, rarely found in cereals. Indian gooseberries are richest source of vitamin C whereas cheapest source is guava.

Vitamin D is an important nutrient as it stimulates mineralization of bone, enhances bone reabsorption, affects collagen maturation, promotes intestinal absorption of calcium and phosphorous and hence affects the normal body growth. Its deficiency has detrimental effects in children aged six months to two years as it causes rickets and hence there is reduced calcification of bone. Bony deformity (curved legs, deformed pelvis, and pigeon chest), tetany, muscular hypotonia and convulsions are related to hypocalcaemia. In adults vitamin D deficiency leads to osteomalacia affecting women more than men especially during pregnancy and lactation. Recommended Dietary Allowances for adults is 600-800 IU/d.[44] Journal of American Medical association reported a range of 700-800 IU/d reduces the risk the fractures and dose of 400 IU/d is not as effective.[45] Sources are sunlight and foods of animal origin such as egg yolk, cheese, butter, fish (salmon and swordfish). The richest source is fish liver oil. Vitamin D is formed by UV rays of sunlight acting on 7-dehydrocholesterol that is in abundance in skin.

Vitamin K is also required for bone metabolism, is a coenzyme for glutamate carboxylase which mediates in conversion of glutamate to carboxyglutamate. Carboxyglutamate attracts calcium ions and absorb into hydroxyapetite. The major non collagenous protein present in bone matrix during bone formation is Osteocalcin and 30% (approximately) of it is present in circulation which is used as an indicator of bone formation results in increase in undercarboxylated osteocalcin,. Studies have shown association of high fracture risk and low BMD due to low Vitamin K intake.[46] However its supplementation lessens the bone turnover and hence improves the overall bone strength. A recent study by Shea et al found low intake of Vitamin K is more to have articular cartilage and meniscal damage progression after three years.[47]

The evidence on Vitamin B thiamine, riboflavin, niacin and cobalamin and bone health is scanty. One study on orthopaedic patients suggested thiamine was found to be deficient among patients with femoral neck fracture but not seen in elective total hip replacement patients.[48] In an experimental study B_2 and its photoproducts found the beneficial effects on cell proliferation and alkaline phosphatase activity and decreased the ratio of RANKL/ osteoprotegerin by enhancing the expression of OPG in the preosteoblastic MC3T3-E1 cells.[49]

A study in pre- and post-menopausal Japanese women suggests a positive correlation related to Niacin and BMD at the calcaneus.[50]

Pyridoxine is a cofactor in several enzymes and is involved in the metabolism of glycogen, phospholipids, and amino acids and is essential for the enzymatic action of lysyl oxidase in cross-linking formation of collagen.[51] However some researchers found that B_6 pyridoxine may act as a substrate of alkaline phosphatase in bone formation and has a role in the coupling of osteoblasts and osteoclasts.[52,53]

Cobalamin B_{12} along with folate B_9 is required for synthesis of DNA. Vitamin B_{12} deficiency is associated with megaloblastic anaemia and demyelinating lesions of spinal cord. A cross-sectional study on patients undergoing hip arthroplasty found that lower serum levels of Vitamin B_6, B_9, and B_{12} were significantly associated with lower serum level of bone forming marker the “osteocalcin”.

CONCLUSION

There is strong association between intake of several nutrients and bone formation and its strength. The vitamins along with minerals, proteins have a direct impact on bone health. The overall physical well-being and bone health is dependent on adequate nutrition.

Recommended nutrition status is a critical factor for overall bone health. Several researches and studies on role of nutrients and bone have found a positive correlation between nutrients and bone formation, preventing bone loss and fractures.

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