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A DIETRY GUIDE TO PREVENTION AND MANAGEMENT OF OSTEOPOROSIS

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ABSTRACT: Osteoporosis is a debilitating disease that affects many older people. Characterized by low bone mass and microarchitectural deterioration (MAD) of bone tissue, Fragility fractures are the hallmark of osteoporosis. There are potentially numerous nutrients and a dietry component that can influence bone health. Bone mineral consists of calcium phosphate, and phosphorus is as important as calcium in supporting bone augmentation and maintenance. Although typical adult diets contain abundant phosphorus, 10% to 15% of older women have intakes of less than 70% of the recommended daily allowance. Patients at the highest risk for fractures benefit from many approved treatments which can be given orally {alendronic acid, risedronatesodium, zolendronic acid, denosumab, raloxifene, hormone replacement theory (HRT)} which results in increased bone mineral density and reduction of fracture risk. This article initially overviews osteoporosis, including its definition, etiology, and incidence, and then provides some information on possible dietry strategies for optimizing bone health and preventing osteoporosis. The potential benefits of calcium, Vitamin D, Vitamin K, phosphorous and Vitamin C are briefly discussed, along with the different treatments, with particular emphasis on the evidence base for their benefits to a bone. It also highlights the importance of some dietry factors for bone health in childhood and adolescence. Osteoporosis can be prevented by proper lifestyle modification like exercise and diet.

INTRODUCTION: Osteoporosis is a systemic disease of skeleton, characterized by reduction of bone mass and concurrent deterioration of bone structure. Consequently, bones become more fragile and there is increased risk of fractures [1], Osteoporosis is not exclusive to older age. It is however one of diseases preventable by adequate nutrition and physical activity. Bone is metabolically active organ. Puberty, as well as infancy is a period of life with most intensive bone growth: 90% of bone mass will have formed by the end of adolescence.

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In the first 5 - 6 years of life, around 100 mg of calcium is retained daily for bone formation, up to 400 mg or even more during puberty. After adolescence, absorption of calcium declines, in young adults daily absorption of calcium amounts to maximally 150 mg. Percentage of calcium absorption from the intestine reaches 75% in infancy, it is between 20 - 30% in adults and declines in further with increasing age [2].

Osteoporotic fractures constitute a major public health problem. Currently in United States alone, 10 million individuals already have osteoporosis, and further 34 million more have low bone mass, placing them at increased risk from this disorder [3]. Moreover, 1in 8 European union (EU) citizens over the age of 50 years will fracture their spine this year [4].

Prevention of Osteoporosis with Calcium: Of all the nutrients necessary for metabolism of bone and

bone density, calcium is the best researched and documented one [1]. Its effect has been proven in many prospective studies, interventional and clinical trails, which all agree, that optimal calcium intake increases bone density in children and adolescents, maintains bone density in adults and slows down its loss in post-menopausal women. Children and adolescents, who often have insufficient time calcium intake, grow faster when supplemented with calcium. Calcium is required for normal growth and development of skeleton[5]. Adequate calcium intake is critical to achieving optimal peak bone mass and modifies the rate of bone loss associated with ageing [6].

Over past decade, convincing evidence has emerged with respect to effects of dietry calcium in bone health in all age groups [4]. The absorption of dietry calcium in foods is also a critical factor in determining the availability of calcium for bone development and maintenance. There is therefore a need to identify food components and/or functional food ingredients that may positively influence calcium absorption to ensure that calcium bioavilability from food can be optimized [7]. A meta-analysis of observational studies relating calcium intake to fracture risk [8] also failed to show any association between calcium and hip fracture, although there was suggestion that individuals with extremely low calcium intake may be increased fracture risk.

Prevention of Osteoporosis with Vitamin D: Vitamin D found naturally in very few foods: endogenous synthesis of Vitamin D, therefore, which occurs when skin is exposed to UVB radiation from sunlight during summer, is a principal determinant of Vitamin D status. however, in latitudes above 40^{o} N and 40^{o} S (Rome, for example, is at latitude 42^{o} N), the dermal photo-conversion of the precursor 7-hydro-cholesterol to Vitamin D occurs little if at all during most of the 3 - 4 winter mo, with this period being extended to 6 mo in more northern latitudes[9]. Vitamin D deficiency is characterised by inadequate mineralization or demineralization, of the skeleton. In children, severe Vitamin D deficiency results in inadequate mineralization of skeleton causing rickets, whereas in adults, it leads to a mineralization defect in skeleton causing Osteomalacia.

In addition, secondary hypothyroidism associated with low Vitamin D status enhances mobilization of calcium from the skeleton [5]. Increasing Vitamin D intake can significantly reduce risk of bone fracture in older people [10].

Prevention of Osteoporosis with Phosphorus: Phosphorus intake does not seen to influence skeletal homeostasis within normal ranges of intake (RDA 700 mg/d) [11], adequate phosphorus intake is essential for bone building during growth and low serum phosphate will limit bone formation and mineralization [12]. Phosphorous deficiency may be marker of general nutritional inadequacy, similar to protein deficiency seen in elderly, and I that regard could lead to an increased risk of fracture. These low phosphorous intake or negative phosphorus balance due to food phosphorus being bound to supplemental calcium may create a relative phosphorus deficiency, which could limit osteoblast function and enhance osteoclastic bone resorption [13]. At any age, the ratio of phosphorus to calcium is probably most important than the intake of phosphorus alone [13 - 14].

Prevention of Osteoporosis with Vitamin K: Recently, the identification of γ-carboxyglutamyl (Gla)-containing proteins in bone, notably osteocalcin and matrix Gla protein, has generated much interest in the role of Vitamin K in bone metabolism and bone health [15]. The circulating concentration of under-γ-carboxylated osteocalcin, a sensitive marker of Vitamin K nutritional status [16], has been reported to be an indicator of hip fracture [17 - 18] and a predictor of BMD [5, 19]. In the Nurses' Health Study, Vitamin K1 intakes of, 109 μg/d were associated with an increased risk of hip fracture in 72,327 women [20]. In the Framingham Heart Study, elderly men and women in the highest quartile of Vitamin K1 intake (median 254 μg/d) had significantly lower adjusted relative risk of hip fracture than did those in the lowest quartile of intake (median 56 μg/d) [21].

In terms of proof of causality, there is a general consensus that there is a need for well-designed, randomized Vitamin K1 supplementation trials in adults to confirm observational findings and the role of Vitamin K in bone metabolism and mass in healthy subjects [22]. Vitamin K has the potential to be a functional food ingredient for bone health.

Of interest, Braam *et al*., showed that relatively high-dose Vitamin K1 supplementation (1 mg/d) for 3 y, if co - administered with calcium, magnesium, zinc, and Vitamin D, reduced post-menopausal bone loss at the femoral neck [23]. The dose of Vitamin K used in this study, however, is unlikely to be achieved by dietary means and would require either supplementation or the functional food approach.

Prevention of Osteoporosis with Vitamin C: Vitamin C is an essential cofactor for collagen formation and synthesis of hydroxyproline and hydroxylysine. Rich dietary sources of Vitamin C include citrus fruit and juices, peppers, broccoli, and tomato products and green leafy vegetables. Epidemiologic studies show a positive association between Vitamin C and bone mass; low intakes of Vitamin are associated with a faster rate of BMD loss, and one study found that higher Vitamin C was associated with fewer fractures; however, there are no randomized clinical trials [24 - 31]. Recommended intakes of 5 or more servings of fruits and vegetables should supply enough Vitamin C for bone health.

Prevention of Osteoporosis with Potassium: The main importance of potassium is based on the influence of potassium on calcium homeostasis, particularly the urinary conservation and excretion of calcium. Low potassium diets increase urinary calcium losses and high potassium diets reduce it. Potassium is found in several vegetables, fruits, legumes, and milk and tends to have alkaline ash characteristics. Higher potassium intake, primarily from fruits and vegetables, was associated with higher baseline BMD and less bone loss [32]. The need to ensure adequate potassium intake from fruits and vegetables is a strong rationale for the "5 to 10 servings per day recommendation" [33].

Prevention of Osteoporosis – Practical Recommendations:

- ✓ Consume daily at least 3 portions of milk and dairy produce with reduced fat content.
- ✓ Choose vegetables with high calcium content (broccoli, cabbage).
- ✓ Drink mineral water with high calcium content.
- ✓ Moderate your alcohol intake.
- ✓ Eat fish at least once a week.
- ✓ Limit consumption of foods and drinks high in phosphates.
- ✓ Use spices in place of salt to enhance flavor (chives, parsley).
- ✓ Eat vegetables and fruit five times daily.
- ✓ Limit consumption of foods high in oxalates.
- ✓ Ensure sufficient intake of Vitamin D (fish, livers, milk), Vitamin K (leafy vegetables, livers, fish) and Vitamin C.
- ✓ Engage in regular physical activity.
- ✓ Do not smoke.
- ✓ Limit salt intake.

Treatment of Osteoporosis: The aims of treatment of established osteoporosis are alleviation of symptoms and reduction of the risk of further fractures. Currently available drugs can prevent further bone loss and reduce the risk of further fractures by up to 50%. Drug treatments should be monitored by BMD or bone turnover marker measurements.

Drugs to Increase or Maintain Bone Mass: Most drugs approved for use in osteoporosis inhibit bone resorption, but some of these (*e.g.* hormone replacement therapy (HRT), bisphosphonates) increase BMD by 5 - 10% over the first 2 years of treatment. We can try to prevent osteoporosis in people who have osteoporosis but not yet a fracture (primary prevention) and people who have already had a fracture (secondary prevention). These treatments are usually given for secondary prevention and treatment according to the National Institute of Health and Care Excellence guidance [36 - 37]. The National Osteoporosis Guideline Group recommends the FRAX™ tool to guide the use of BMD testing and preventive drugs according to clinical variables including the patient's age.

Calcium and Vitamin D Treatment: Calcium 1000 mg/day and Vitamin D 800 IU/day given together have been shown to prevent hip fracture in housebound, elderly patients. This treatment is safe and inexpensive, and does not require monitoring. It is commonly given with other treatments for osteoporosis. There has been some concern about an increased risk of cardiovascular disease with calcium supplementation, so it is wise to encourage obtaining adequate calcium from the diet, if possible [34].

Alendronic Acid: It is given in a dose of 10 mg/day continuously or 70 mg once weekly. It must be taken at least 30 minutes before breakfast (to help absorption) with a full glass of water, and the patient must not lie down for at least 30 minutes after taking the tablet (to avoid Oesophagitis). Alendronic acid is equally effective for the hip, forearm and spine, and has been shown to prevent fracture at all these sites.

Zoledronic Acid: This drug is given by intravenous infusion (5 mg over 15 min) every 12 months. It reduces fractures of the spine and hip and all other fracture sites; it has also been shown to reduce further fractures in patients presenting with hip fractures.

Denosumab: It is given at a dose of 60 mg every 6 months by subcutaneous injection. It has been shown to reduce the risk of spine, hip and non-spine fractures. After stopping treatment, there is a rebound increase in bone turnover markers; therefore it should be given at intervals of no less than 6 months, and another drug should be started as soon as it is withdrawn to prevent this increase in bone turnover and a likely increase in the risk of vertebral fractures.

Raloxifene: Raloxifene is given in a dose of 60 mg/day continuously. Raloxifene has been shown to reduce the risk of spine (but not other) fracture, and can reduce the risk of breast cancer. However, it can increase the risk of deep vein thrombosis and does not prevent hot flushes.

Hormone Replacement Theory (HRT): HRT is an effective treatment for osteoporosis even in elderly women. However, compliance and acceptability are often low in older patients, and the observation that HRT is associated with increased risk of stroke and ischaemic heart disease means that it is no longer routinely used for the treatment of osteoporosis. It is still used up to the age of 50 years in women with early or premature menopause.

- **Testosterone Therapy:** This therapy is effective in men with hypogonadism. Three other agents can be useful in special circumstances, for example intolerance of other agents:
- **Strontium Ranelate:** It works by mechanisms that are not yet fully elucidated. It reduces the risk of spine and non-spine fracture and is given in a dose of 2 g/day in water. However, it increases the risk of cardiovascular disease so should not be given to patients at risk of this. Following these cardiovascular concerns, strontium ranelate will no longer be available in the UK after August 2017.
- **Calcitonin:** Intranasally has recently been withdrawn by the Medicines and Healthcare products Regulatory Agency for use in osteoporosis. Its use has been associated with an increased risk of cancer.
- **Calcitriol:** It stimulates calcium absorption and may stimulate osteoblasts directly. It appears to be effective in corticosteroid-induced osteoporosis, in which it can be considered an alternative to HRT or bisphosphonates, particularly in younger patients. Regular monitoring of serum calcium is required because hypercalcaemia is a common adverse effect.

Long - Term Treatment with Bisphosphonates: The bisphosphonates have an excellent safety record. However, there have been case reports of osteonecrosis of the jaw (particularly after tooth extraction) and atypical femur fractures (subtrochanteric or femoral shaft stress fractures) that might be caused by long-term use. Experts [34 - 38] have proposed that oral bisphosphonate therapy be continued for up to 5 years and intravenous therapy up to 3 years; if bone density of the femoral neck is then above −2.5, treatment is stopped and bone density (or bone turnover markers) measured every 2 years until bone loss resumes. If the bone density is −2.5 or lower, the bisphosphonate should be continued up to 10 years and then stopped. Bisphosphonates such as alendronic acid and zoledronic acid suppress bone turnover and prevent bone loss for several years after they have been stopped.

CONCLUSION: Osteoporosis is a multifactorial disease, the risk of which can be reduced by adequate nutrition and appropriate lifestyle. Prevention should start in childhood, as that is the time, when bone formation is very intensive and achievement of optimal peak bone mass is a

necessary requirement for optimal bone density in older age. Optimal intake of calcium, Vitamins D and K are important factors in primary as well as in secondary prevention of osteoporosis. Kidneys and the intestine have a limited capability to adjust the metabolism of calcium in response to actual requirements of the organism. When certain substances in food reduce intestinal absorption or increase excretion by the kidney, the organism can utilize compensatory mechanisms, to prevent adverse effect on bone.

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