Nutritional aspects of the prevention and treatment of osteoporosis

Aspectos nutricionais na prevenção e no tratamento da osteoporose

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SUMMARY

Osteoporosis is a global health problem characterized by low bone mass and microarchitectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture. Nutrition plays a critical role in reducing the risk of osteoporosis through its effect on all of these fragility factors, especially on the development and maintenance of bone mass. An adequate calcium, vitamin D and protein intake resulted in reduced bone remodeling, better calcium retention, reduced age-related bone loss, and reduced fracture risk. Recent evidence indicates that a healthy dietary pattern including dairy products (mainly fat free), fruit and vegetables and adequate amounts of meat, fish and poultry is positively related to bone health. Furthermore, mineral and vitamin supplementation should be closely monitored by health professionals since it could have adverse effects and be insufficient to ensure optimal protection of bone health. Arq Bras Endocrinol Metab. 2010;54(2):179-85

Keywords

Osteoporosis; bone mass; nutrition intake; calcium; vitamin D; protein

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SUMÁRIO

A osteoporose é um problema de saúde global, caracterizada por baixa massa óssea e deterioração da microarquitetura do tecido ósseo, com consequente aumento da fragilidade óssea e suscetibilidade a fraturas. A nutrição desempenha um papel fundamental na redução do risco de osteoporose por seu efeito sobre todos os fatores relacionados à fragilidade óssea, principalmente no desenvolvimento e na manutenção da massa óssea. Uma adequada ingestão de cálcio, vitamina D e proteína leva à redução da remodelação óssea, à maior retenção de cálcio, à redução da perda óssea relacionada à idade e à redução do risco de fraturas. Evidências recentes indicam que uma alimentação saudável, incluindo a ingestão de produtos lácteos (principalmente os desnatados), frutas e verduras, e uma quantidade adequada de carnes, peixes e aves, está relacionada positivamente com a saúde óssea. Além disso, a suplementação de vitaminas e minerais deve ser monitorada de perto, por profissionais de saúde, uma vez que pode ter efeitos adversos e ser insuficiente para assegurar uma eficaz proteção à saúde óssea. Arq Bras Endocrinol Metab. 2010;54(2):179-85

Descritores

Osteoporose; massa óssea; ingestão alimentar; cálcio; vitamina D; proteína

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INTRODUCTION

Osteoporosis is defined as a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture (1). Osteoporosis is a global health problem, with the accelerating growth of the older population, it is estimated that 52 million people will suffer from osteoporosis or osteopenia by 2010 (1).

After age 50, 1 in 2 women and 1 in 4 men will have an osteoporosis-related fracture (1). Osteoporotic fractures involve a number of factors beyond bone weakness; including falls, slow reflexes, sarcopenia, and inadequate soft tissue padding. Nutrition plays a critical role in reducing the risk of osteoporosis through its

effect on all of these fragility factors, especially on the development and maintenance of bone mass. Maintaining optimal nutrition and weight bearing activities have been shown to reduce the risk of osteoporosis by as much as 50% (2).

It is believed that genetic factors determine up to 80% of peak bone mass with the remainder influenced by environmental factors such as exercise, smoking, medication and nutrition (3). Good nutrition, especially with protein, calcium and vitamin D, is also important for preserving bone mass and strength in adults and the elderly. In addition, attention to nutrition is an important component of a successful rehabilitation program in patients who have had an osteoporotic fracture. In frail elderly patients who have sustained hip fractures this is crucially important, as poor nutritional status can slow down recovery and increase susceptibility to further fractures (4).

CALCIUM

The mineral calcium plays a major role in bone strength and is of prime nutritional importance in osteoporosis, being essential for bone health throughout life (5).

The primary role of calcium in the body is structural, providing the rigidity necessary for the skeleton and teeth to function mechanically. Bone contains about 99% of the body's calcium. Calcium in body fluids also exerts critical metabolic functions, binding to proteins, and operating as a signal transmitter and protein activator within cells. Muscle contraction and nerve transmission are two of the many body functions that rely on calcium for activation. Additionally, calcium is also involved in blood clotting (6).

Calcium is required for normal growth and development of the skeleton (1). Adequate calcium intake is critical for achieving optimal peak bone mass and modifies the rate of bone loss associated with aging (1). Over the past decade, convincing evidence has emerged with respect to effects of dietary calcium on bone health in all age groups. Unfortunately, there is a significant proportion of some population groups failing to achieve the recommended calcium intakes in a number of Western countries (7).

After menopause, changes in sex hormone levels and nutrition are associated with an increase in bone remodeling, leading thereby to an increase in bone fragility. Epidemiological studies report that a lifetime of high calcium intakes can reduce fracture risk by as much as 60% (8). In adults, obligatory calcium losses have to be offset by sufficient calcium intakes and efficacious intestinal absorption. Otherwise, bone is used as a source of calcium to maintain homeostasis in extracellular calcium concentration (9).

In a review of 52 calcium intervention studies, 50 showed that increasing calcium intakes resulted in reduced bone remodeling, better calcium retention, reduced age-related bone loss, and reduced fracture risk. The review also reported that out of 86 observational studies, 64 reported relationships in favor of increased calcium intakes, with reduced fracture risk, bone loss or improved bone mass. While most of the investigator-controlled studies used calcium supplements, six used dairy sources of calcium; all were positive. Most of the observational studies were also based on dairy calcium, and approximately 75% supported the conclusion that increased calcium from dairy foods is protective of the skeleton (10).

The positive effects of calcium supplementation have essentially been ascribed to a reduction in bone remodeling. However, calcium supplements may be associated with mild gastrointestinal disturbances such as constipation, flatulence, nausea, gastric pain, and diarrhea. Calcium may also interfere with the intestinal absorption of iron and zinc (9). Additionaly, it has been reported that calcium supplementation in healthy postmenopausal women was associated with an increased risk of cardiovascular events in women with more than 80 years of age and a previous cardiovascular event (11). Postmenopausal women received 1,000 mg/day of calcium supplementation plus an intake of approximately 860 mg/day of calcium from the diet. However, such amount is considered too high to be applied in clinical practice. These observed effects indicate that the use of calcium supplements should be considered only when the intake of this nutrient is below the recommended level for each stage in life.

Recommended daily calcium intakes for populations vary between countries, often as a result of differing use and interpretation of the available scientific data (12). The recommendations for calcium intake in mg/day from several countries are shown in table 1.

Milk and other dairy foods are the most readily available sources of calcium in the diet. Dairy foods have the additional advantage of being good sources of protein and other micronutrients (besides calcium) that are important for bone and general health. Other good food sources of calcium include certain green vegetables (e.g. broccoli, curly kale, bok choy); whole canned fish with soft, edible bones such as sardines or

pilchards; nuts; and tofu set with calcium (4). Some examples of the approximate calcium levels in foods are shown in table 2.

Table 1. Recommendation for calcium intake in mg/day from several countries

Country/Organization	Adults		Elderly	
	Men	Women	Men	Women
Australia	800	800	800	1,000
European Community	700	700	700	700
FAO/WHO	1,000	100	1,300	1,300
Mexico	800	800	800	800
United Kingdom	700	700	700	700
Food Nutrition Board	1,000	1,000	1,200	1,200
Japan	600	600	600	600

FAO/WHO: Food and Agriculture Organization of the United Nations/World Health Organization. Adapted from Looker (12).

Table 2. Approximate calcium levels in foods

Food	Serving size	Calcium (mg)
Milk, whole	236 mL/8 fl oz	278
Milk, semi-skimmed	236 mL/8 fl oz	283
Milk, skimmed	236 mL/8 fl oz	288
Yoghurt, low fat, plain	150 g/5 oz	243
Yoghurt, low fat, fruit	150 g/5 oz	210
Cheese, cheddar type	40 g/medium-size chunk	296
Cheese, cottage	112 g/4 oz	142
Cheese, mozzarella	28 g/1 oz	101
Cheese, Camembert	40 g/average portion	94
Ice cream, dairy, vanilla	75 g/average serving	75
Tofu, soya bean, steamed	100 g/3.5 oz	510
Soya drink	236 mL/8 fl oz	31
Soya drink, calcium-enriched	236 mL/8 fl oz	210
Broccoli, cooked	112 g/4 oz	45
Curley kale, cooked	112 g/4 oz	168
Apricots, raw, stone removed	160 g/4 fruit	117
Orange, peeled	160 g/1 fruit	75
Figs, ready to eat	220 g/4 fruit	506
Almonds	26 g/12 whole	62
Sardines, canned in oil	100 g/4 sardines	500
Whitebait, fried	80g/average portion	688
Bread, white, sliced	30 g/1 medium slice	53
Bread, wholemeal, sliced	30 g/1 medium slice	32
Pasta, plain, cooked	230 g/medium portion	85
Rice, white, basmati, boiled	180 g/medium portion	32

Adapted from International Osteoporosis Foundation, 2006 (4).

Although some other plant foods also contain appreciable amounts of calcium, some contain substances that bind to the calcium and prevent it from being absorbed, e.g. compounds called oxalates in spinach and rhubarb, and phytates in dried beans, cereal husks and seeds (13). However, oxalates and phytates only bind the calcium in the foods they are in – they do not interfere with calcium absorption from other foods or drinks. Calcium-fortified foods and drinks, including breads, cereals, orange juice and soy beverages are also available in some countries, as are various commercial brands of mineral waters which can contain significant amounts of calcium. Soy beverages are sometimes called 'soy milk', but it is important to look for the ones that are fortified with calcium, because soy drinks do not naturally contain calcium (4).

VITAMIN D

Vitamin D is also essential for the development and maintenance of bone, both for its role in assisting calcium absorption from the diet, and for ensuring the proper renewal and mineralization of bone tissue (4).

Vitamin D deficiency is characterized by inadequate mineralization, or demineralization, of the skeleton. In adults, severe vitamin D deficiency leads to a mineralization defect in the skeleton causing osteomalacia (4). In addition, the secondary hyperparathyroidism associated with low vitamin D status enhances mobilization of calcium from the skeleton (4). There is a considerable body of evidence that vitamin D deficiency is an important contributor to osteoporosis through less efficient intestinal absorption of calcium, increased bone loss, muscle weakness, and a weakened bone microstructure (14).

Increasing vitamin D intake can significantly reduce the risk of osteoporosis and bone fracture in older people. A recent study of Caucasian postmenopausal women from the National Osteoporosis Risk Assessment study (NORA) reported that lifetime current vitamin D intakes were also associated with reduced risk for osteoporosis over three years, OR 0.73 (95% CI: 0.66-0.81) (15). In a meta-analysis realized for Bischoff-Ferrari and cols. in 2005 (16), the antifracture efficacy of oral vitamin D supplementation in older persons was evaluated. The author showed that vitamin D intakes of 700-800 IU/day reduced the relative risk of hip fracture by 26% and any nonvertebral fracture by 23% compared with calcium or placebo. No significant

benefit was observed in double-blind randomized control trials with intakes of 400 IU vitamin D/day.

Scientific evidence suggests that on a global level, vitamin D insufficiency is widespread, even in very sunny regions such as the Middle East, Latin American and Asian countries, and in Australia. This is clearly demonstrated in a cross-sectional observational international study in 1,285 community-dwelling, postmenopausal women with osteoporosis, in 18 countries. The prevalence of vitamin D inadequacy (defined as < 30 ng/mL) was over 50% in all five world regions, and was highest in the Middle East (81%) and Asia (63%) (17). In Brazil, a cross-sectional study evaluated serum levels of 25-hydroxyvitamin D [25(OH)D] in the elderly living in the city of São Paulo, the authors observed that 71.2% of the inpatient group and 43.8% of the outpatient group had 25OHD levels below the minimum recommended (50 nmol/L) (18). Vitamin D insufficiency was also observed in 24% of women with osteoporosis (19).

However, optimal serum concentrations of 25(OH) D have not been defined. A recent review summarized evidence from studies that evaluated thresholds for serum 25(OH)D concentrations in relation to bone mineral density (BMD), lower-extremity function, dental health, and risk of falls, fractures, and colorectal cancer. It was observed that for all endpoints, the most advantageous serum concentrations of 25(OH)D begin at 75 nmol/L, and the best are between 90 and 100 nmol/L (20).

A large part of the population is currently below the 75 nmol/L threshold and could certainly benefit from appropriate vitamin D supplementation. For most patients with vitamin D deficiency, correcting vitamin D serum levels as quickly as possible is the goal. Typically, patients receiving 50,000 IU of vitamin D once a week for 8 weeks will correct vitamin D deficiency (21). Aloia and cols. in 2008 (22), suggest a dose of 3800 IU/day of vitamin D for individuals with serum 25(OH) D levels above 55 nmol/L and a dose of 5000 IU/day for those below that threshold, with the purpose to attain a serum 25(OH)D concentration > 75 nmol/L. Mosekilde suggests that in adults, a minimum dietary intake of 700-1000 IU/day is necessary to achieve levels between 75 and 100 nmol/L (23).

A recent paper by Cashman and cols. (24), recommends that the vitamin D intake necessary to maintain the vast majority (97.5%) of elderly aged ≥ 64 years of age during winter with serum 25(OH)D levels > 80 nmol/L should be of 1,548 IU/day. Estimated dietary vitamin D requirements at selected percentile in elderly aged ≥ 64 years of age to maintain serum 25(OH)D concentrations above selected biochemical cutoffs during winter are shown in table 3.

Table 3. Estimated dietary vitamin D requirements at selected percentile in adults aged ≥ 64 years to maintain serum 25(OH)D concentrations above selected biochemical cutoffs during winter

Serum 25(OH)D cutoff	Percentile			
	50th	90th	95th	97,5th
	IU/day			
> 25 nmol/L	-	104	232	344
> 37.5 nmol/L	-	448	576	688
> 50 nmol/L	284	736	872	988
> 80 nmol/L	860	1,328	1,464	1,548

IU: International Unit. Adapted from Cashman and cols. (24).

Very little vitamin D is naturally present in our food, which includes oily (or fatty) fish such as salmon, tuna, sardines and mackerel, egg yolk and liver. In some countries, fortified foods specifically labeled as such, including milk and other dairy foods, margarine, and breakfast cereals, are viable options (4). Some examples of the approximate vitamin D levels in foods are shown in table 4.

Table 4. Approximate vitamin D levels in foods

Food	Mg per serving	IU per serving	% RNI (for ages 51-65 years)*
Cod liver oil**, 1 tbsp	23.1	924	231
Salmon, grilled, 100 g	7.1	284	71
Mackerel, grilled, 100 g	8.8	352	88
Tuna, canned in brine, 100 g	3.6	144	36
Sardines, canned in brine, 100 g	4.6	184	46
Egg, hen, average size, 50 g	0.9	3	9
Liver, lamb, fried, 100 g	0.9	36	9
Margarine, fortified, 20 g	1.6	62	16
Bran Flakes***, average serving, 30 g	1.3	52	13

* The RNI (recommended nutrient intake) for adults, ages 51-65 years. The RNI is defined by the FAO/WHO as "the daily intake which meets the nutrient requirements of almost all (97.5%) apparently healthy individuals in an age- and sex-specific population group". Daily intake corresponds to the average over a period of time. ** Fish liver oils, such as cod liver oil and halibut liver oil, also contain appreciable amounts of vitamin A, which can be toxic if consumed in excess. *** Bran Flakes are given as an example of a vitamin D-fortified breakfast cereal.

Adapted from International Osteoporosis Foundation, 2006 (4).

PROTEIN

Protein should be the central part of a complete diet for adults. While physical growth occurs only for a brief period of life the need to repair and remodel muscle and bone continues throughout life. Maintaining the

health of muscle and bone is an essential part of the aging process and critical to maintain mobility, health and the active tissues of our body (25).

Protein is also a key constituent of bone tissue and therefore an adequate dietary supply is essential (4). The majority of the observational studies support a positive association between protein intake and bone health. There are several epidemiological studies, both cross-sectional and longitudinal that have reported an association between dietary protein and bone (26-28). These studies reveal that individuals who consume the most dietary protein have the highest BMD. In addition, prospective studies have observed that individuals with the highest protein intake have the slowest rate of bone loss (26,29).

One of the mechanisms by which dietary protein may improve bone mass can be explained by the fact that increasing dietary protein is also known to increase circulating levels of insulin-like growth factor 1 (IGF-1), and conversely, a low-protein diet decreases IGF-1 (30). IGF-1 is a key mediator of bone growth but also has a role in the skeletal response to anabolic Parathyroid Hormone (PTH) therapy (31). Increasing dietary protein from 0.85 to 1.55 g/kg per day resulted in lower markers of bone resorption and higher circulating levels of IGF-1 in healthy older men and women (32).

Dietary proteins would induce systemic acidosis and thereby would promote bone mineral dissolution (33). Increasing protein intake may increase acid production and renal acid excretion as a consequence of protons released during the oxidation of sulphur-containing aminoacids such as methionine, cysteine and cystine (9). An acidic environment affects bone in several ways, and an acidogenic (high-protein) diet induces calciuria (34).

The administration of alkaline salts of potassium can be used to reverse the negative effects of acidogenic diets. A randomized, placebo-controlled, double-blind study showed that in older adults, potassium bicarbonate attenuates the protein-induced rise in urinary nitrogen excretion and may promote calcium absorption in subjects with both low and high protein diet intake (35). In another double-blind, controlled trial study, it was observed that potassium bicarbonate had a favorable effect on bone resorption and calcium excretion, suggesting that increasing the alkali content of the diet may attenuate bone loss in healthy older adults (36).

On the other hand, it has been hypothesized that increasing dietary protein in humans results in higher urinary calcium. In fact, previous calcium balance studies did not show an improvement in calcium absorption (even with high protein intake), the increase in urinary calcium was assumed to be of bone origin, which leads to the hypothesis that high protein diets are detrimental to the skeleton (37). However, a recent study demonstrated that the increase in urinary calcium excretion is due to improved intestinal calcium absorption, and high protein diets do not result in negative skeletal calcium balance (37,38).

However, as described above, higher protein intakes are associated with improvements in BMD and skeletal metabolism in the elderly. Furthermore, many protein-rich foods such as meat and dairy foods are also rich in phosphorus and potassium, both of which have an opposing effect in that they tend to prevent urinary calcium loss (39). Finally, some aminoacids promote calcium absorption which would also offset urinary losses, and as long as calcium intake is adequate, higher protein intakes have been shown to improve bone density (37).

Mounting evidence suggests that the Recommended Dietary Allowance (RDA) for protein of 0.8 g/kg per day is not optimal for bone health in elderly people. Reassessments of the nitrogen balance studies show that a protein intake of 1.0 to 1.3 g/kg per day is needed to offset the typically lower energy intake and impaired insulin response in elderly individuals (40). Moderate protein diets of 1.0 to 1.5 g/kg per day are shown to be associated with normal calcium homeostasis without altering bone metabolism (37). These data seem to indicate that doubling the RDA from 0.8 g/kg per day to 1.5 to 1.6 g/kg per day may result in better muscle and bone health in elderly individuals. Although this level is approximately twice the current RDA, it is still within the acceptable range of intake (10%-35% of total calories) (41). Based on these data, a recommendation of 1.0 to 1.2 g/kg per day of proteins (or approximately 13%-16% of total calories) would maintain normal calcium metabolism and nitrogen balance without affecting renal function.

In summary, the majority of scientific evidence – including that from clinical trials – supports beneficial effects of protein intake on bone health, and highlights the risks associated with protein insufficiency and malnutrition.

MAGNESIUM AND PHOSPHORUS

Approximately 60% of the magnesium (Mg) in the body is in bone. Mg influences mineral metabolism indirectly through its role in ATP metabolism and as a cofactor

for over 300 proteins, the calciotropic hormones and $1,25(OH)_2D$. Mg also influences bone health by direct effects on bone quality, decreasing hydroxyapatite crystal size, thereby preventing the larger, more perfect mineral crystals that cold lead to brittle bone (42). Severe experimental magnesium deficiency results in abnormal bone structure and function, but this level of depletion is rarely observed in generally well nourished human populations (43). Magnesium is fairly widespread in the food chain; particularly good sources include green vegetables, legumes, nuts, seeds, unrefined grains, and fish (4). Recent studies have found a positive association between fruit and vegetable consumption and bone health (44,45). However, there are no studies to date which demonstrate that magnesium supplementation is useful either in preventing bone loss or reducing fracture risk (4). The majority of the phosphorus in the body is found as phosphate (PO_4). Approximately 85% of the body's phosphorus is found in bone. Phosphorus is found in most foods because it is a critical component of all living organisms. Dairy products, meat, and fish are particularly rich sources of phosphorus. Phosphorus is also a component of many polyphosphate food additives and is present in most soft drinks as phosphoric acid (42).

Some investigators are concerned about the increasing amounts of phosphates in the diet. Because phosphorus is not as tightly regulated by the body as calcium, serum phosphate levels can rise slightly with a high phosphorus diet, especially after meals. High phosphate levels in the blood reduce the formation of the active form of vitamin D (calcitriol) in the kidneys, reduce blood calcium, and lead to increased PTH release by the parathyroid glands. However, high serum phosphorus levels also lead to decreased urinary calcium excretion (46). If sustained, elevated PTH levels could have an adverse effect on bone mineral content, but this effect has only been observed in humans on diets that were high in phosphorus and low in calcium. Moreover, similarly elevated PTH levels have been reported in diets that were low in calcium without being high in phosphorus (47). A controlled trial in young women found no adverse effects of a phosphorus-rich diet (3,000 mg/day) on bone-related hormones and biochemical markers of bone resorption when dietary calcium intakes were maintained at almost 2,000 mg/day (48). At present, there is no convincing evidence that the dietary phosphorus levels experienced in the U.S. adversely affect bone mineral density. However, the substitution of phosphate-containing soft drinks and snack foods for milk and other calcium rich foods does represent a serious risk to bone health.

CONCLUSIONS

Bone health rests on a combination of several factors including on an adequate dietary pattern. Recent evidence indicates that a healthy diet with adequate amounts of protein, calcium, vitamin D, and nutrients that promote a more alkaline ambience such as potassium, would favor bone metabolism. In this regard optimal protection of bone requires a diet rich in dairy products (mainly fat free), fruit and vegetables and adequate amounts of meat, fish and poultry. Furthermore, mineral and vitamin supplementation should be closely monitored by health professionals since it could have adverse effects and be insufficient to ensure optimal protection of bone health.

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