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Impact of suplementation vitamins D, C and K on osteoporosis

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Abstract

Osteoporosis is a skeleton disease characterized by a decrease in bone mass, disturbance of their microarchitecture and reduction of bone mineral density (BMD). Decreased bone quality is manifested by a higher risk of fractures, but bone pain and lowering of growth may occur earlier, although osteoporosis may occur asymptomatically before the fracture occurs. It is a disease of older people, affects 25 to 30% of postmenopausal women, while morbidity among men over 50 is around 8%. Bone tissue is subject to continuous remodeling as a result of resorption processes (release of minerals from the tissue) regulated by osteoclast activity and bone matrix construction by absorption of mineral components to maintain quality and bone mass resistance. In this study attention will be focused on the impact of vitamin supplementation on the development of osteoporosis

Key words: **osteoporosis, vitamins supplementation, treatment, influence**

Introduction

Osteoporosis is the result of disturbances in the metabolism of bone remodeling. Morbidity increases with age due to the decrease in the possibility of maintaining normal bone mass due to the aging of the body. Bone growth is the most intense in adolescence, it is significantly slowed after the age of 20, however, many studies sugested that bone mass can increases up to 35 years of age [1]. After reaching this age, the process of involution begins, in other words, the inevitable depletion of bone mass and a decrease in the quality of the skeleton. In postmenopausal women, this process accelerates. Studies mention, the annual loss of bone mass ranges from 1% to 3% per year, but in some cases may even exceed 3%. In men, the bone mass loss process is much slower. The risk factors for the development of osteoporosis is most in eldery age, in the group at risk of disease are women over 65 who are four times more likely and men who reached the age of 70. Lifestyle plays a big role in the prevention of osteoporosis,low low physical activity increases the risk of osteoporosis. The low BMI index correlates positively with the incidence of osteoporosis. The most important nutritional factors predisposing to osteoporosis are insufficient supply of calcium and vitamin D, inadequate supply of phosphorus and disturbed ratio of the amount of calcium to phosphorus consumed. Other factors are deficiencies of vitamin C and K and magnesium deficiency [2]. Too high a supply of protein and vitamin A increases the risk of osteoporosis. This review focuses on determining the effect of the supply of vitamins involved in bone metabolism, i.e. vitamin D, C and K on the prevention of osteoporosis, and the ability to inhibit the progression of bone resorption by introducing appropriate dietotherapy. The role of individual vitamins in the processes of bone formation and resorption will be discussed, followed by the results of studies assessing the effect of vitamins on parameters related to the quality of bone tissue and the risk of osteoporosis.

MATERIALS AND METHODS

Thirteen observational and experimental studies (including randomized clinical trials) from the years 2000-2019 are indicated in this review. The studies evaluating the effects of suplementation of only vitamins, which affected in bone metabolism (with the exception of the part dealing with vitamin D due to insufficient number of studies focused on calciferol nutritional interventions without additional calcium supplementation), the exclusion criteria was presence of

interventions with other nutrients or pharmaceuticals. Age of participants in all studies> 50 years, these were both healthy and suffering from osteoporosis and osteopenia.

Vitamin D

Vitamin D is definied as several fat-soluble compounds belonging to the group of steroids, which is responsible for the preservation of calcium homeostasis, phosphorus and magnesium, and for a number of other processes, e.g. immunomodulatory. The two most widely described in the literature substances are vitamin D_2 (ergocalciferol) and vitamin D_3 (cholecalciferol), they differ from each other in the possition of the side chain. It is allowed to use the name calciferol in relation to both of them. The biologically active form of vitamin D is the 1α,25-dihydroxyvalalferol, which is occur in result of metabolism changes [3].

The daily requirement for calciferol for an adult is around 15 μg for both men and women. Vitamin D_2 is eaten together with plant foods or fungi, while vitamin D_2 is found in foods of animal origin. The richest sources of cholecalciferol are fatty fish, fish oils and eggs, and sources of ergocalciferol include yeast and some fungal species. Vitamin D is also found in fortified food, we can meet it in fat spreads. It is estimated that the daily intake of vitamin D with a diet is only 2.5-5 μg / day, therefore supplementation of this vitamin is recommended from October to April [4]. However, calciferol is synthesized by the skin during exposure to the sun. In this way, 80% of the demand is covered.

Absorption of vitamin D takes place in the gut, then connects to a specific carrier protein (gc globulin) and is taken up from the blood through the liver, followed by hydroxylation catalyzed by the enzyme 25-hydroxylase of vitamin D, because calciferol is not an active biological substance. In addition to the liver, hydroxylation also takes place in the kidneys, cartilages and intestines [5]. 1α, 25-dihydroxycalciferol has a multidirectional effect on the body's metabolism. It has an effect on the nervous system, stimulates the immune system by increasing the expression of genes encoding peptides with antibacterial activity [6]. In addition, vitamin inhibits the process of apoptosis and tumor cell angiogenesis. Vitamin D affects the absorption of calcium in the intestines. Under conditions of calcium deficiency, calciferol participates in the process of active calcium absorption, increasing its bioavailability. In hypocalcimia, it increases the resorption of calcium and phosphates [7].

Vitamin C

Vitamin C is a water-soluble chemical compound from the group of polyhydric alcohols. Another name for this compound is ascorbic acid, its acid character is due to the presence of hydroxyl groups. It has strong antioxidant properties. The human body can't synthesize ascorbic acid by itself. The daily requirement for this vitamin is 75 mg for an adult woman and 90 mg for an adult male per day. Ascorbic acid is found in fruits and vegetables such as black currants, broccoli, spinach, lemon and orange [4]. Ascorbic acid plays a key role in the synthesis of collagen, affecting the activity of proteins responsible for the hydroxylation of proline. Vitamin C takes part in the synthesis of neurotransmitters, e.g. norepinephrine, also participates in the processes of building myelin sheaths, and protects the nervous system by removal of free radicals. In addition, ascorbic acid has a significant effect on the bone tissue metabolism. Affects the fate of osteoblasts and their proliferation. It plays a key role in creating the matrix of collagen tissue, and is active in the process of osteocalcogenesis [8**].**

Vitamin K

Vitamin K is actually a group of fat soluble biologically active substances derivatives of 2-methyl-1,4-naphthoquinone. In the scientific literature, we can usually read about two chemical compounds - finochinon (K_1) having a fityl residue in the third position, and menaquinone (K_2), which distinguishes from the form K1 the presence of the isoprenoid side chain also in the third position. There is also a third form having no side chain - menadione (K_3), which is a synthetic analogue [12]. The daily requirement for vitamin K for an adult male is at the level of 65 μg for an adult male and 55 μg for females [7]. Vitamin K must be supplied with the diet, sources of finochinon (K1) are vegetables such as: spinach, broccoli, kale, lettuce. Whereas menachinone (K2) is synthesized by human intestinal bacteria, it also occurs in products such as eggs, meat and milk and its products [13]. Absorption of vitamin K1 takes place in the small intestine, the absorption mechanism uses active transport, while the absorption of menaquinone requires no energy expenditure and takes place in the large intestine. Vitamin K is a fat-soluble substance, which is why chylomicrons and lipoproteins (ApoA, ApoB-48, ApoC and ApoE) are involved in its transport to the liver. Vitamin K leaves the liver in combination with VLDL, apolipoprotein B-100, C and E, and then penetrates osteoblasts due to the presence of receptors for lipoproteins such as LDLR and LRP1 [21]. The body is not able to store large amounts of vitamin K, hence it must be supplied on a regular basis with the diet. The body requies them to maintain normal

blood clotting through participation in hepatic synthesis of blood coagulation factors [9]. Vitamin K is a coenzyme for enzymatic reactions of protein synthesis regulating the synthesis of prothrombin, coagulation factor VII, IX, X. Vitamin K plays a very important role in maintaining bone strength, because it acts as a cofactor of gamma carboxylase - an activating enzyme dependent on vitamin K proteins such as OC, Gla protein, S protein and GAS6 protein. They are responsible, among others for the synthesis of new osteons, bone mineralization and bone calcium metabolism [11]. In addition, vitamin K mobilizes the formation of bone tissue, and inhibits bone resorption processes also through a mechanism unrelated to gamma carboxylase [12]. In addition, many studies have shown that the correct intake of vitamin K has a beneficial effect on bone mineral density (BMD).

RESULTS

Vitamin D

Calciferol plays a important role in the phosphate-calcium economy. Vitamin D deficiency may contribute to the deterioration of skeletal structure by reducing the absorption of calcium in the intestines [13].

Table 1. Results of vitamin D intervention *own source* [16]

Authors	n	Group	Method	Time	Results
Robin M Daly and others 2009 [15]	167	Health men in age >50	Fortified milk (1000 mg Ca^{2+}+ 800 IU D_3/day)	2 years	Decreased bone mass and BMD reduction
Peacock M. and others 2000 [17]	367	Women at age >60	Vitamin D (15 mcg/day) Ca^{2+}(750 mg/day)	4 years	Slight decrease in bone resorption, slower reduction in BMD, prevention of secondary hyperparathyroidism in the vitamin D group
Grados F. and others 2003 [18]	192	Women at age >65	Vitamin D (400 IU/day) Ca^{2+}(500 mg/day)	1 year	Increase of BMD, decrease NTX, CTX, ALP in supplementation of vitamin D group
Erik Roj Larsen and others 2003 [19]	9605	Males and females in age >66	Vitamin D_3(400 IU/day) Ca^{2+}(1000 mg/day)	4 years	16% fewer fractures in the group included in the supplementation program compared to the control group

It is presumed that the therapeutic effect of vitamin D supplementation is poorly noticeable, and the benefits of optimal supply are closely related to the improvement of calcium absorption [14]. For this reason, most interventions are based on supplementation of both vitamin D and calcium. Low levels of vitamin D are associated with a higher incidence of osteoporosis [15].

A number of studies have demonstrated the effectiveness of vitamin D supplementation in combination with calcium in the treatment of osteoporosis.

Vitamin C

Table. 2 Results of vitamin C intervention *own source* [16]

Authors	**n**	**Group**	**Method**	**Time**	**Results**
Sahni S. 2009 [20]	958	Males and females in eldery age	Supplementation of vitamin C (average intake 313 mg/day)	17 years	Significantly less fractures in the group with high intake of vitamin C
Min Hee Kim 2016 [21]	3047	Males and females in age >50	Assessment of intake of vitamin C in traditional diet	4 years	Negative correlation between the risk of osteoporosis and the intake of vitamin C
Sagiura M. and others 2009 [22]	187	Females in postmenopausal age	Assessment of intake of vitamin C in traditional diet	4 years	Significantly slower drop in BMD in the group with high intake of vitamin C compared to the low supply group
Kim YA. and others 2009 [23]	1196	Females in postmenopausal age, and females with osteoporosis	Assessment of vitamin C intake, which uses 24 hours intake method	2 years	Positive correlation between vitamin C intake and BMD, lower intake of vitamin C in the osteoporotic group

An adequate supply of ascorbic acid reduces the risk of fractures in the elderly population [20]. The higher intake of vitamin C in the daily food ration reduces the risk of developing osteoporosis. The lower concentration of vitamin C in plasma is associated with a decrease in BMD [21] [22]. Adequate supply of ascorbic acid promotes the preservation of bone mass and bone mineral density [23]. The observed correlations are the result of the presence of ascorbic acid in many processes of tissue synthesis, and antioxidant activity that protects tissues from the harmful effects of free radicals.

Vitamin K

Is well known fact, vitamin K has a significant effect on bone tissue metabolism. Its proper supply promotes the preservation of beneficial bone mineral density, inhibits the bone resorption process and stimulates the synthesis processes of new tissues.

Table 3. Results of vitamin K intervention *own source* [16]

Authors	**n**	**Group**	**Method**	**Time**	**Results**
Yasui T and others 2006 [24]	34	Women in postmenopausal age affects with osteoporisis/osteopenia	K_2(45 mg/day) K_2(45 mg/day) i D_3(0,75 mcg/day)	1 year	Decrease of ucOC in bouth groups, decrease of OC and BALP in group with addition of vitamin D
Cheung AM and others 2008 [25]	440	Women in postmenopausal age affects with osteopenia	K_1(500 mcg/day) vs. placebo	4 years	Decrease of ucOC and level ofOC, no difference in level of CTX
Ushiroyama T. and others 2002 [27]	172	Health women in postmenopausal age affects with osteoporosis/osteopenia	MK-4 (45 mg/day)	2 years	Increase %BMD in 18-24 month of observations
Koitaya N. and others 2013 [28]	50	Health women in postmenopausal age	MK-4 (1,5 mg/day) vs. placebo	1 year	Not differences in BMD
Knapen MHJ and others 2013 [29]	244	Health women in postmenopausal age	MK-7 (180 mcg/day) vs. placebo	3 years	Significantly lower decrease of body heitght in group MK-7

UcOC – Correlation of Undercarboxylated Osteocalcin; OC – Osteocalcin; BALP – Bone-specific Alkaline Phosphatase; CTX – C-terminal Telopeptide; BMD – Bone Mineral Density

Studies from 2002-2013 investigating the effectiveness of vitamin K supplementation have shown that such intervention may have a positive effect on bone tissue condition. Yasui T and others assessed the bone resorption rates and obtained a decrease in the ucOC index in the vitamin K group [24]. Other studies point to the inverse correlation between ucOC and BMD [25]. Cheung et al. in its 4-year study also showed the effect of vitamin K supplementation on the decrease in ucOC and OC [26]. The prerequisites for affecting bone mineral density (BMD) are unclear. In the study of a group of women suffering from osteoporosis or osteopenia, an increase

in BMD was observed after 18 months of supplementation with vitamin K (MK-4) [27], however, Koitaya N. and others in 2013 found no differences in BMD in relation to MK-4 supplementation [28]. Decrease in body height is an indicator of bone loss and development of osteoporosis, it is also positively correlated with the frequency of bone fractures. Knapen's MHJ et al. research showed that supplementation MK-7 can slow down the process of body height loss [29].

DISSCUSION

There are mentions about the influence of the correct supply of vitamins and minerals in adolescence (during the predominance of bone formation processes on resorption) to a decrease in the risk of osteoporosis. 2% higher skeletal mass in adolescente correlates with a 20% lower risk of osteoporosis in eldery age [30]. The diet of many polish people is characterized by inadequate supply of vitamins and minerals. In addition which in combination with high consumption of alcohol and tobacco increases the risk of bone disease. Data indicate a deficit in vitamin D in 89% of young women in the winter [31], and a significant part of the Polish population also has too low a level of vitamin C intake [32]. Increase people's awareness of the impact of nutrition and lifestyle on the risk of civilization diseases is necessary. Greater awareness of health threats will favorably influence the development of eating habits. Parents education is very important because the mother's and father's eating habits have a tremendous impact on shaping their children's lifestyle. Studies included in this review prove the effectiveness of vitamin supplementation in the treatment of osteoporosis. The population-program of vitamin D supplementation showed a positive effect for bone quality in eldery people, and contributed to decrease amount of fractures [22]. Running more similar programs should reduce morbidity of osteoporosis.

CONCLUSIONS

Correct level of vitamin D, C and K intake have a beneficial effect for quality of bone tissue. Supplementation with calcium and calciferol has a positive effect on bone mineral density, lowers bone resorption rates and reduces the risk of fractures. The therapeutic effect is noticeable in healthy people as well as those suffering from osteoporosis. The intake of vitamin D and calcium at an appropriate level throughout life is an important factor in the prevention of

osteoporosis. Studies showed a significant relationship between the intake of vitamin C and the condition of bone tissue. Intake of vitamin C should be controlled during osteoporosis treatment. Most studies on the influence of vitamin K on the development of osteoporosis indicate an inverse correlation between the adequate supply of vitamin K and the markers of osteoporosis development. Vitamin K slows down the disease and shows effectiveness in the prevention of bone disease. The exact mechanism of the effect of vitamins on bone metabolism has not yet been recognized. Further investigations are needed.

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