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THE ROLE OF VITAMIN D IN THE PREVENTION OF OSTEOPOROSIS IN MENOPAUSAL WOMEN

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Annotation: The analysis was based on 5 randomized controlled trials for hip fracture risk (n=9294) and 7 randomized controlled trials for non-vertebral fracture risk (n=9820). All studies used cholecalciferol. A daily vitamin D intake of 700 to 800 IU was found to reduce the risk of hip fracture by 26% (3 randomized controlled trials with 5572 subjects; hazard ratio - RR = 0.74; 95% confidence interval i - CI 0.61–0.88) and 23% compared with placebo or calcium for non-vertebral fractures (with 6098 subjects 5 randomized controlled trials; RR = 0.77; 95% CI, 0.68–0.87). Low-dose (400 IU) vitamin D (2 randomized controlled trials with 3,722 participants; RR for hip fracture, 1.15; 95% CI, 0.88 to 1.50; RR, 1.15% CI); 0.8–1.24) [8].

In 2009, a meta-analysis of randomized controlled trials was published to determine the effectiveness of vitamin D supplements and active forms of vitamin D in preventing falls in older adults with and without calcium supplements. Databases include Medline, the Cochrane Register of Controlled Trials, and BIOSIS. The analysis included eight randomized controlled trials (n=2426), with a mean age of 65 years, who received a fixed dose of vitamin D tablets: vitamin D (cholecalciferol) or vitamin D (ergocalciferol) or an active form of vitamin D (1 - α-hydroxyvitamin D (1-α-hydroxycalciferol) or 1,25-dihydroxyvitamin D3 (1,25-dihydroxycholecalciferol). There was homogeneity between studies regarding vitamin D doses (p =0.02), however, patients were divided into two groups based on the achieved concentration of 25(OH) vitamin D. With different doses of vitamin D during therapy: 25 (OH) - vitamin D concentration less than 60 nmol / l (deficiency) and more than 60 nmol / l normal (p = 0.005) application of high doses of vitamin D resulted in a 19% reduction in the risk of falls (RR = 0.81, 95% CI 0.71 to 0.92; n=1921 in seven studies), with a serum 25(OH)-vitamin D concentration of 60 nmol/L or above that, the risk of falling was reduced by 23% (RR=0.77, 95% CI 0.65 to 0.90). In the background of low doses of vitamin D (RR=1.10, 95% CI 0.89 to 1.35; n=505) or 25(OH)-vitamin D concentration less than 60 nmol/l (RR=1, 35, (95% CI 0.98 to 1.84) was not found to reduce the risk of falls. Two randomized controlled trials (n = 624) using active forms of vitamin D met the inclusion criteria. Treatment with active forms of the vitamin reduced the risk of falls by 22% (RR = 0.78, 95% CI 0.64 to 0.94). Thus, the authors concluded that a daily intake of 700-1000 IU of vitamin D reduced the risk of falls by 19% in the elderly, as was the case with treatment with active forms of vitamin D [7]. A daily dose of vitamin D below 700 IU does not reduce the risk of falls in the elderly [10].

Key words: Prevalence and role of calcium and vitamin D deficiency as risk factors for AP and fractures.

According to the 2010 North American Menopause Society (NAMS), the minimum dose of vitamin D is 800 IU [27]. The serum vitamin D concentration needed to reduce the risk of fractures should be higher than 20 ng/ml, and to reduce the risk of falls - from 20 to 30 ng/ml [10, 12]. A blood level of 25(OH)-vitamin D less than 10 ng/ml (25 nmol/l) is usually diagnosed as osteomalacia [20]. However, according to the

recommendations of the US National Institute of Medicine, the daily intake of vitamin D should be 600 IU for persons under the age of 71, and 800 IU for those 71 and older. At the same time, for the population of North America, vitamin D deficiency is a concentration of the latter from 12 to 20 ng / ml. A value of 20 ng/ml is accepted as a biologically reasonable norm, which was recorded in 97.5% of patients without osteoporosis [14]. In Canada, the recommended dose of the drug for people over 50 years of age has been increased from 800 to 2000 IU per day [31]. In the clinical guidelines of the Russian Osteoporosis Association, the recommended dose of vitamin D is 800 IU per day [2].

In a randomized, placebo-controlled, double-blind study conducted by MF Holik, 1000 IU of vitamin D or vitamin D supplementation daily for 3 months resulted in a 10 ng/ml increase in blood vitamin D levels. shown. 18, 22]. The study involved 68 healthy people aged 18 to 84 from the Boston area. 60% of patients were vitamin D deficient (vitamin D concentration less than 20 ng/ml) and 87% were deficient (less than 30 ng/ml), approximately 47% of patients received 400 IU vitamin D and multivitamins. approximately 47% of subjects received 1.2 cups of milk. All participants were randomized into 4 groups: a placebo group that received 1,000 IU of vitamin D or vitamin D or a combination of 500 IU of vitamin D and 500 IU of vitamin D. For 11 weeks, the authors analyzed the dynamics of vitamin D concentration in blood serum. After 3 months, no significant changes in the level of vitamin D were noted in the placebo group, an increase in the concentration of vitamin D by 10 ng / ml was found in the groups that received 1000 IU of vitamin D daily, i.e. A daily intake of 1000 IU of vitamin D was associated with an increase in vitamin D concentration of 10 ng/ml. However, since the initial blood vitamin D level was 19 ng/ml, none of the subjects had a vitamin D concentration greater than 30 ng/ml. It appears that both children and adults require 2,000–3,000 IU per day to maintain vitamin D levels above 30 ng/ml in the absence of sunlight [22].

A number of studies have shown that during bisphosphonate therapy, patients with low levels of vitamin D initially had a low increase in BMD, i.e. To achieve the maximum antiresorptive effect from taking bisphosphonates, the level of vitamin D in the blood should be within the reference values.

After intensive therapy with vitamin D (500,000 IU for 5 weeks) diagnosed with vitamin D deficiency, the level of the latter reached normal values in 17 (85%). Of the 20 patients with insufficient vitamin D concentrations associated with a significant increase in BMD in the spine and femoral neck (3.0 and 2.7%, respectively); $p<0.2$). In patients with reduced vitamin D levels

A subsequent loss of BMD was noted. In a clinical study conducted by D. Grigori et al., it was also found that the rate of increase in BMD depends on the initial concentration of vitamin D [17]. Similar results were obtained in the work conducted by S. Adami et al. After 13.1 months of antiresorptive therapy (alendronate, risedronate, raloxifene), more than 75% of patients with postmenopausal osteoporosis were included in the study. Optimal vitamin D saturation has been shown to maximize the response to antiresorptive therapy for changes in BMD and fracture prevention in older postmenopausal adults ($p=0.004$). In a retrospective analysis by A. Deane et al. [13] also showed a lower BMD increase ($p = 0.04$) in patients with low levels of vitamin D at baseline during bisphosphonate therapy.

Thus, studies conducted in recent decades have convincingly confirmed that vitamin D is an underappreciated and long-neglected, absolutely necessary for human health and survival [6, 19, 25]. The consequences of vitamin D deficiency are manifested in insufficient development and function of bones, disruption of neuromuscular transmission, which leads to falls and fractures [9].

Osteoporosis (OP) is a systemic skeletal disease characterized by decreased bone strength and increased fracture risk. In the European Union, approximately 21% of women aged 50–84 years have AP according to WHO criteria [1]. In Western Europe, postmenopausal women have a 40% incidence of fractures in the localization typical for AP, which is higher than the incidence of breast cancer (12%) and is close to the incidence of cardiovascular disease. According to the Federal Center for the Prevention of AP in the

Russian Federation, 33.8% of women aged 50 and older living in cities have AP, 43.3% have osteopenia, and 24% already have fractures. The results of bone densitometry in a random sample of 45-70-year-old postmenopausal women in the Moscow region showed that opacity was detected in 26% of women in the spine, in the femoral neck and proximal femur - in 12%. In addition, 52-58% of subjects have osteopenia in these areas [3, 4]. Extrapolation of available epidemiological data to the population of the Russian Federation shows that AP affects 14 million people in the Russian Federation (about 10% of the country's population) and another 20 million people have osteopenia. In the Russian Federation, 7 vertebrae are broken every minute, and 1 femur is broken every 5 minutes.

Calcium and vitamin D preparations are widely used in the prevention and complex treatment of AP, but despite extensive and long-term experience in studying the effectiveness and safety of this type of therapy, no consensus has been reached regarding the optimal doses. potential risks, as well as whether calcium and vitamin D should be used together, whether vitamin D supplementation is sufficient, and whether additional bioactive substances (collagen, micro and macronutrients) are needed to enhance the effects of vitamin D . and calcium. In reviewing the literature, we tried to answer these questions based on the analysis and synthesis of modern scientific data.

Sources of calcium and vitamin D for humans

A person receives 70-80% of calcium from dairy products, they also contain other components such as phosphorus and magnesium, which have a positive effect on bone remodeling processes [6], phosphoproteins from the main milk proteins [7], casein and estrogens [6]. 8]. Therefore, getting enough calcium from dairy products is an important factor in maintaining bone health [9, 10]. In their review, DA McCarron and RP Heaney (2004) estimate that in the United States alone, consuming dairy products within the recommended limits would result in $209 billion in budget savings due to reductions in health and social benefits, of which $14 billion would result in cost savings. came to the conclusion that it will come. Treatment of fractures in patients with AP [11].

Vitamin D is a fat-soluble vitamin that is synthesized in humans from 7-dehydroxycholesterol in the skin by exposure to ultraviolet light or obtained from certain foods. The production of vitamin D3 depends on the severity of skin pigmentation, the width of the region, the length of the day, the time of year, weather conditions, and the area of skin not covered by clothing. For example, in countries located in northern latitudes, most of the ultraviolet radiation is absorbed by the atmosphere in winter, and vitamin D3 is almost not synthesized between October and March [13]. Another important source of vitamin D is food. Oily fish (cod, tuna, etc.) are especially rich in vitamin D [13]. Ergosterol, a precursor of vitamin D, is found in mushrooms and yeast. When dried in the sun or exposed to ultraviolet light, ergosterol in mushrooms is converted to vitamin D2 [14].

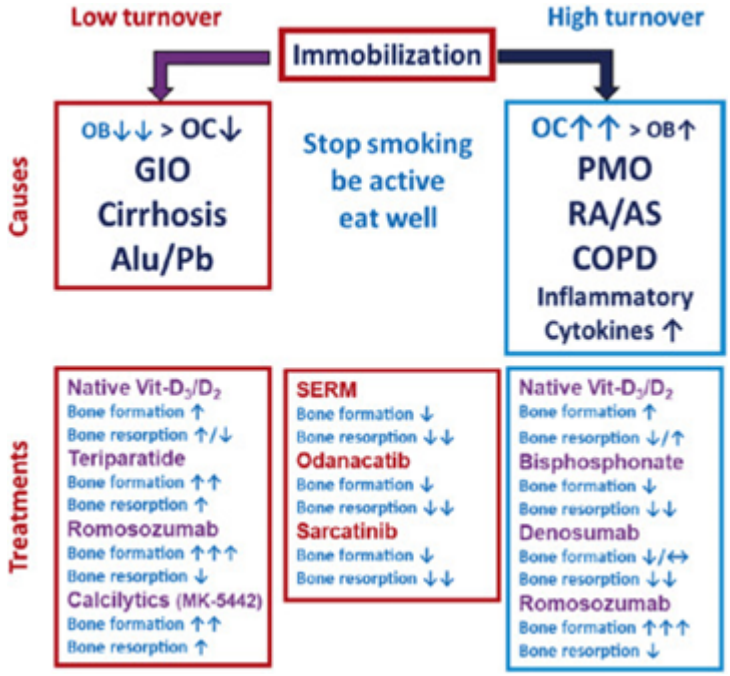
After 2 successive hydroxylation reactions in the kidneys, vitamin D forms an active metabolite, 1,25(OH)2D3 - D-hormone, which binds to specific receptors of organs and tissues, and vitamin D has a biological effect related to its effect.

Prevalence and role of calcium and vitamin D deficiency as risk factors for AP and fractures The average amount of calcium for women aged 19-50 and men aged 19-70 is 1000 mg/day, for women over 50 and men over 70 - 1200 mg/day [15, 16]. According to the interim results of the Russian osteoscreening program, the average intake of calcium in women and men is 683±231 and 635±276 mg, respectively. Only 9% of women and 6% of men consume 50% or less of the daily calcium requirement in most cases. An analysis of the level of calcium consumption in food products among 1,712 residents of the Moscow region aged 20-87 years showed that 42.3% of women consume dairy products once a day, 33.7% less than once a day consume or do not consume at all, and only 24% of women include dairy products in their diet several times

a day. All age groups 40 years and older show deficient calcium intake, with minimal intake after 80 years of age [18].

In patients with AP and in people with osteopenia, the level of calcium intake is much lower than in the healthy population - 901 mg/day versus 715 mg/day, respectively [19]. Another risk group for insufficient calcium intake in our country can be considered medical workers: a survey conducted among 842 doctors aged 20-72 in 16 regions showed that their average calcium intake moli is only 445 mg per day, and a deficiency has been found in intake. in 90% of cases [19].

Calcium deficiency is an important risk factor for the development of AP and fractures [20-22]. Low calcium intake is associated with significant social consequences of hip fracture, so increasing dairy consumption may be effective in reducing the adverse health effects of hip fracture in the general population [23]. In addition to beneficial effects on bone mineral density (BMD) and moderate antiresorptive effects, adequate calcium intake in postmenopausal women is associated with a reduced risk of colorectal cancer, hypertension, kidney stones, and obesity [24].



Men and women under 70 should get at least 600 IU per day, and those over 70 should get at least 800 IU per day [25]. The prevalence of vitamin D deficiency increases significantly in old age. With aging, the time spent in the sun and the skin's ability to synthesize vitamin D3 decrease, and the level of 1,25(OH)2D produced in the kidneys due to impaired kidney function decreases - all of which contribute to its prevalence. prevalence of vitamin D deficiency in the elderly. In particular, Russian studies have shown high levels of vitamin D deficiency among postmenopausal women in Moscow [26] and elderly residents of the Ural region [27]. Because vitamin D is essential for adequate calcium absorption and normal bone metabolism, chronic deficiency leads to secondary hyperparathyroidism, increased bone resorption, and rapid loss of BMD, and is associated with an increased incidence of falls.

Efficacy of calcium and vitamin D supplementation in preventing AP and fractures: monotherapy or combination?

Food should be the main source of calcium [1, 24]. However, due to the apparent deficiency of calcium intake from food sources, the appropriateness of calcium salts supplementation is questioned. There are separate studies on the positive effect of calcium supplements on BMD and the risk of fractures, but in

general, calcium in the form of monotherapy combined with vitamin D is characterized by weaker clinical potential in the prevention and complex treatment of AP. [28, 29]. Some evidence suggests that adequate postmenopausal calcium intake slows bone loss due to estrogen deficiency and even reduces the risk of bone fractures [25, 30]. In particular, R. Recker et al. (1996) concluded that 600 mg of calcium per day for 4 years in independent living elderly women reduced the risk of developing vertebral fractures, especially if there was a history of such fractures (in the treatment group versus the placebo group, risk). fracture 2 .45, 95% confidence interval (CI) 1.42–4.20) [30]. A meta-analysis of 59 articles published by B. Shea et al. (2000) showed that monotherapy with calcium salts has a positive effect on BMD only at high doses - 2-3 g per day, and there are no reliable data on the positive effect of calcium monotherapy on fracture incidence.]. In addition, according to the results of a recent meta-analysis, the use of calcium supplements without concomitant vitamin D intake is associated with a 30% increased risk of myocardial infarction [32]. In this regard, the amount of calcium obtained from any source should not exceed the age-recommended norm, and calcium salts should be used together with vitamin D preparations [1, 20].

Vitamin D supplementation at a dose of 700–800 IU per day was associated with a statistically significant reduction in the risk of fractures and falls [33, 34]. In particular, MC Chapuy and others. (1994) demonstrated daily calcium (1200 mg) and vitamin D (800 IU) intake in elderly women living in nursing homes for 18 months. reduces the risk of proximal femoral fractures by 43% and all non-vertebral fractures by 32%; The 3-year use of this combination resulted in a mean reduction in hip fracture risk of 27% (relative risk = 0.73, 95% CI 0.23–0.99) [35] . In addition, 2 meta-analyses have shown that vitamin D supplementation is associated with a reduced risk of cardiovascular disease and death [36].

A meta-analysis by S. Boonen et al. (2007), 9 randomized clinical trials involving a total of 53,260 patients showed that vitamin D monotherapy without calcium supplementation had no significant effect on fracture risk, particularly hip fracture [37]] . The same study convincingly showed that the combined use of calcium and vitamin D reduced the risk of hip fracture by 25% (95% CI 4–42) and the risk of all peripheral fractures by 23% (95% CI 1–40). vitamin D with monotherapy [37]. Similar data were obtained from a pooled analysis of 7 studies including 68,517 patients (mean age 69.9 years). In both cases, calcium therapy with vitamin D at a dose of 10-20 and 10 mg per day has been shown to be more effective than vitamin D monotherapy at a dose of 10, in particular, in reducing fracture risk. -20 mg/day [38]. Also, several studies have shown that vitamin D monotherapy without calcium supplementation is not associated with a reduction in the risk of fractures at different sites or even the risk of falls [41] compared to placebo [39, 40]. A cost-minimization analysis of taking calcium and vitamin D preparations conducted in Russia showed that the cheapest of the combined preparations containing calcium and vitamin D is the preparation Calcium-D3 Nycomed Forte [42].

Calcium Plus Vitamin D: Do You Need More?

Combined preparations of calcium and vitamin D sometimes contain an additional complex of minerals and trace elements. There is limited evidence that supplementation of certain vitamins and minerals may slow bone loss in postmenopausal women [43]. Similar data have been obtained for magnesium, boron, fluoride, vitamins C and K, so these supplements may be beneficial for postmenopausal women and adults [43].

A number of results have also been obtained regarding the role of some minerals and vitamins in the synthesis of bone collagen. The strength of collagen interconnections plays an important role in the biological and biomechanical properties of bone. The properties of these crosslinks in newly synthesized collagen matrix may differ from those in "mature" and "old" bone matrix. Furthermore, these interactions of the newly synthesized matrix may be altered in healthy subjects, AP patients, or diabetic patients, which may account for the decreased bone quality and strength in these diseases. is one [44, 45]].

One study found that treatment with aldecalcidiol (a newly synthesized active metabolite of vitamin D) stimulated enzymatic collagen cross-linking and bone mineralization in primates, but not non-enzymatic cross-linking and bone microdamage. reduces 'planing' [46]. Vitamin C is also an important cofactor for the formation of type 1 collagen and the synthesis of hydroxyproline and hydroxylysine, and additionally maintains the stability of collagen crosslinks through its antioxidant properties. A biological role of silicon in collagen synthesis and maintenance of its stability is also assumed [47].

A study was conducted that showed use for 12 months. A calcium-collagen chelate dietary supplement containing 500 mg of calcium and 200 IU of vitamin D is more effective in slowing bone loss across the entire skeleton than the same doses of calcium and vitamin D combined. In addition, a decrease in the level of sclerostin and tartrate-resistant acid phosphatase, as well as an increase in the activity of the bone fraction of alkaline phosphatase, were observed in the group of patients who received the chelate complex of calcium and collagen. Despite the positive results, the quality of this study does not allow us to draw firm conclusions about the effectiveness of the calcium-collagen chelate complex for the prevention of AP [48].

Summary

Based on the analysis of modern scientific data, it can be clearly stated that calcium and vitamin D deficiency are common and their adequate intake from food sources or drugs should be a mandatory component of AP and fracture prevention. In terms of effectiveness and safety, the use of combined calcium and vitamin D preparations is more suitable than monotherapy with them. The best results in reducing the risk of fractures are observed when prescribing a combination of calcium and vitamin D in a dose of 700-800 IU per day. Despite some data on the effectiveness of some minerals, trace elements and bioactive supplements used to prevent bone loss and the effect on the quality of bone collagen, the independent effect of these bioactive substances on the effectiveness of calcium and vitamin D is not comparable to .

Vitamin D deficiency and deficiency is one of the most common hypovitaminosis in the world. The consequences of vitamin D deficiency are manifested in the insufficient development and functioning of bones and the occurrence of osteoporosis. The gold standard in the treatment of postmenopausal osteoporosis is the use of first-line drugs - bisphosphonates in combination with calcium salts and vitamin D. Currently, the recommended daily intake of vitamin D in most countries is 800 IU, which is not enough in some cases. and the effectiveness of antiresorptive therapy decreases. In this regard, the question of vitamin D doses necessary to correct vitamin D deficiency and deficiency in the treatment of postmenopausal osteoporosis patients remains controversial. The results of these studies highlight the importance of early assessment and correction of vitamin D deficiency/deficiency in patients with osteoporosis.

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