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Review

Vitamin D Dietary Intake through Dairy Products to Reduce the Risk of Osteoporosis

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Abstract: Background: Vitamin D and calcium are the most important dietary compounds that affect bone mass, even if other minerals (potassium, zinc, etc.) and other vitamins (A, C and K) are also involved. Vitamin D, in fact, plays an important role in calcium homeostasis and calcium absorption. Talking about calcium, it is well known the "calcium paradox": hip fractures incidence are higher in western countries, where calcium is frequently included in human diet, while the occurrence of these fractures is lower in developing countries, where diets are normally poor in calcium. This paradox may be partially understood considering vitamin D content in serum of local population; a report produced by WHO/FAO experts team investigating on diet, nutrition and the prevention of specific diseases stated that there is enough clinical data demonstrating that an intake of vitamin D and calcium together sufficient to cover dietary requirements can greatly reduce the risk of osteoporotic fracture in older people. Vitamin D can also act as a hormone; vitamin D2 (ergocalciferol) is derived from the UV-B radiation of ergosterol, the vitamin D precursor naturally found in plants, fungi, and invertebrates. Vitamin D3 (cholecalciferol) is originated by sunlight exposure from 7-dehydrocholesterol, a precursor of cholesterol that can also act as a provitamin D3. Dietary intake of vitamin D is very important when skin is exposed for short times to ultraviolet B light (UV-B) one of the three kind of invisible light rays together with UV-A and UV-C. This can be considered the usual situation in some latitude and in winter season, or the typical condition for older people and/or for people with vey white delicate skin. Actually, the recommended daily intake of dietary vitamin D is strictly correlated with age, ranging from 5 μg for infants, children, teen-agers and adults, including women during pregnancy and lactation, to 15 μg for people over 65 years.

Keywords: vitamin D; calcium; bone mass; osteoporosis; dairy foods; fortified foods

1. Introduction

Vitamins are nutrients characterized by low-molecular weight; these compounds are obtained from external sources in the diet and play a crucial physiological and metabolic role [1]. Vitamins are classified into two categories based on liquid solubility, specifically the water-soluble vitamins (B complex and vitamin C) and the fat-soluble vitamins (A, D, E, and K). Most of the vitamins cannot be synthesized by humans; for this reason, they must be provided by food sources or eating manufactured dietary supplements. Vitamins are bioactive nutrients showing several health-promoting properties which effectively affect human growth and human health; in fact, development of several diseases, including cancer and cardiovascular diseases, can be caused by a severe vitamins' deficiency [2].

Rickets is a condition characterized by a decreased mineralization of bone tissue and growth plates, causing weak bones in infants and children. The word "rickets" was published for the first time in 1634; according to the findings of the Royal Infirmary in Manchester, the best treatment to heal rickets was represented by cod liver oil [3]. Two centuries later the relationship between sunlight and rickets was discovered; studies performed at the British Medical Research Council

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determined that cod liver oil and exposure to sunrays, too, represent good remedies to heal rickets. The term Vitamin D was created in 1922, describing a vitamin able to promote calcium deposition [4].

Vitamin D in nature is available as ergocalciferol (vitamin D2) or cholecalciferol (vitamin D3); considering the essential role performed by this nutrient in calcium metabolism, appropriate amount of vitamin D is necessary for skeletal health during the entire life, and can be provided both from the diet or by cutaneous synthesis induced by sunlight [5]. Vitamin D is synthesized in the skin through exposure to the sun-light, especially the ultraviolet B light of wavelength ranging between 290–315 nm, that are responsible of promoting the conversion of 7-dehydrocholesterol to provitamin D [6]. Vitamin D synthesis induced by sun-light is strictly correlated with the season during the year, the time during the day, the period of exposure, the skin pigmentation and the different latitude. In fact, in extreme latitudes such as beyond 35N or S, vitamin D synthesis is greatly reduced or does not occur during winter season. Moreover, skin synthesis of vitamin D decreases with advancing age, consequently in elderly is higher the percentage of people with low vitamin D levels [7]. Therefore, vitamin D dietary intake must increase in elderly (Table 1), but it is not easy to fulfill this target if the diet is not characterized by vitamin D-rich foods. Fatty fish, fish liver oils and egg yolk represent the most important natural dietary sources of vitamin D, but these foods are not so frequently eaten by most of the people [8]; in meat and offals vitamin D content is normally low (Table 2).

Table 1. Dietary recommendations for vitamin D.

Age	Nutrient intake (μg/day)	Nutrient intake (IU/day)
0-3 months	8.5	340
4-6 months	8.5	340
7-9 months	7	280
10-12 months	7	280
1-3 years	7	280
> 65 years	10	400
Pregnancy	10	400
Lactation	10	400

Source: modified by Lanharn-New et al. [9].

Vitamin D, both obtained from food or produced by cutaneous synthesis, undergoes hydroxylation in the liver to 25-hydroxyvitamin D [25(OH)D] that represents the most abundant circulating form, and later in the kidney is converted into 1,25-dihydroxy vitamin D, which is strictly correlated to the metabolism of calcium and phosphate absorption from the intestine, influencing also bone cells [10]. There is also a direct effect of parathyroid hormone on the production of 1,25-dihydroxy vitamin D, with a specific control of the physiologic conditions necessary to link the active vitamin D to the calcium homeostasis needs [11].

The best method to determine in human body vitamin D level is represented by the detection of serum concentration of 25(OH)D; the optimal level for either skeletal or extra-skeletal health is not the same for everybody but it depends on the specific population tested. Severe lack of vitamin D in adults can cause the development of osteomalacia, a disease characterized by the incomplete mineralization of osteoid, while in children is responsible for rickets [12]. Chronic lack of vitamin D intake is the cause of secondary hyperparathyroidism, that is responsible for an increased bone turnover, with a consequent progressive bone loss and finally an increased risk of bones fracture [13].

Clinical trials performed on patients with hip fracture, in fact, found very low vitamin D levels in these subjects; the findings obtained in all the trials stated that people lacking of vitamin D are

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more subjected to lose muscle mass and can frequently fall down, with an associated increased risk of fractures [14]. The effect of an appropriate vitamin D supplementation in the elderly was a significant decrease of hip and bone fractures, demonstrating clearly the effects of a correct serum vitamin D levels on general skeletal health.

Table 2. Vitamin D3 and 25(OH)-D-3 content in meat and offal.

Foodstuff	Vitamin D3 (µg/kg)	25(OH)-D-3 (µg/kg)
Beef steak	< 0.5	0.8
Beef liver	< 0.5	3.4
Beef kidney	1.3	3.0
Pork fillet	1.1	< 0.6
Pork liver	4.0	4.4
Lamb leg steak	0.4	10.4
Chicken leg	3.0	< 2.0
Chicken fillet	2.0	< 2.0

Source: modified by Lanharn-New et al [9].

2. Osteoporosis

Osteoporosis is a progressive disease caused by the deterioration of the bone structure because of the loss of bone mineral density (BMD); the main effect in people affected by osteoporosis is an increase of the risk of fractures for the rest of the life [15]. Considering the situation of the adult population (over 50 years) in the United States, more than 40 million adults are at high risk of developing osteoporosis because of a low BMD, while the total amount of patients affected by osteoporosis in the States is about12 million [11]. Evaluating the situation in Europe, specifically in Italy, 3,5 million women and 1 million men are affected by osteoporosis; each year are reported 250,000 fractures due to osteoporosis, specifically 80,000 hips and 70,000 femurs [11]. Unfortunately, within year, patients with fracture of the proximal femur show a mortality rate of 15-30%. It is interesting to evaluate the occurrence of osteoporosis in african-americans, who are less affected by this disease compared to white population, and in small white women, that is, according to epidemiological available data, the most affected human category [16].

Low BMD characterizes osteoporosis, with a consequent deterioration of the microarchitecture with trabeculae smallness, associated with reduced mineralization and an increase in cortical porosity [17]. In order to determine the BMD it is necessary to calculate the ratio between bone resorption due to osteoclasts and bone formation due to osteoblasts, during a continuous remodeling process. Considering the period of the growth of children, bone formation requires a ratio in favour of bone growth, with the consequent achievement of peak bone mass when they reach the adult age, in which the BMD normally remains relatively stable; in elderly the activity of osteoclasts increases while that of osteoblasts decreases, causing a loss of bone mass [18].

The occurrence of osteoporosis and osteoporotic fractures is higher in women compared to men [19]; a suggested strategy to reduce the risk of osteoporosis in adult women, improving BMD, is a regular intake of dairy products in childhood and adolescence [20]. Bone health is in fact the result of a combination of dietary factors and, on the other hand, is also strictly correlated to some non-modifiable risk factors associated to osteoporosis, such as age, while in women under 50 years of age must be considered as a main factor the presence of menstruation [21].

Low serum level of vitamin D compared to the feeding requirements can provoke secondary hyperparathyroidism with increased bone turnover, progressive bone loss and consequently a higher risk of bone fracture [22]. Patients with hip fracture typically show very low vitamin D serum levels [23]; vitamin D supplementation in the elderly reduces the occurrence of hip and bone

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fractures, confirming the effect of adequate serum vitamin D levels for general skeletal health. The importance of satisfying vitamin D requirements in order to obtain the best response in BMD is stated in the guidelines for the management of postmenopausal osteoporosis, in which are described recommendations for its supplementation [14], together with calcium, especially for women [24].

3. Vitamin D and Cancer

Cancer incidence and mortality rate show different data according to the specific area in the world; for this reason, ecological studies have been performed in order to better understand the correlations to the ultraviolet-B (UVB)–vitamin D–cancer hypothesis. In the United States, for example, annual sunlight doses are strictly correlated with the map of colon cancer mortality rates [25]. The UVB vitamin D cancer hypothesis was proposed at the beginning of these studies because vitamin D synthesis caused by sunlight is the most important physiological effect for humans, therefore vitamin D probably represents the mechanism correlating sunlight to reduced risk of cancer [26]. The ecological studies later investigated also on the incidence of breast and ovarian cancer.

The UVB–vitamin D–cancer hypothesis has also been applied to evaluate the correlation among cancer incidence and serum 25(OH)D levels; the results showed significant inverse correlations for breast and colorectal cancer [26]. In a clinical trial performed on mice, UV exposure showed a significant stronger effect in reducing progression of colorectal cancer tumors compared to oral vitamin D administration, even if both the treatments increased the 25(OH)D contents [27].

Another approach to determine how vitamin D can affect cancer risk is represented by three different types of observational studies: case–control (CC), prospective or nested case–control (NCC), and cross sectional. In CC studies, 25(OH)D levels are determined close to the time of cancer diagnosis and then are compared with those obtained in the controls. Cross-sectional studies need long time normally since cancer diagnosis, so serum 25(OH)D levels could be different from values detected before diagnosis.

Genetic polymorphism studies have also been performed. Considering the changes occurring in serum 25(OH)D levels, alternative methods to determine how vitamin D affects cancer risk have been developed. Most of vitamin D's actions regarding cancer are performed by the hormonal metabolite of vitamin D, 1,25-dihydroxyvitamin D, affecting gene expression through activating vitamin D receptors (VDRs). According to this reason, studies of cancer risk involving VDR polymorphisms can be very interesting.

The pharmaceutical drug model has been used in clinical trials aimed to understand if vitamin D could decrease cancer risk. Really, this study model is not appropriate for studies involving vitamin D because the two basic assumptions of drug trials are not satisfied. In fact, firstly people receive vitamin D from UVB exposure, from diet and also from supplements, and secondly the dose–response relationship is not linear, consequently serum 25(OH)D concentrations vary widely among different people for the same vitamin D supplement intake, because of the effects due to the different body mass indexes and also because of the different baseline 25(OH)D levels [28]. It is important to consider that most of the people involved in the trials were characterized by relatively high baseline 25(OH)D concentrations or, on the other hand, did not receive high enough vitamin D doses to modify significantly 25(OH)D concentrations along the health outcome–25(OH)D concentration relationship [27].

Several ecological studies evaluating cancer incidence and mortality rates showed clearly that solar UVB is correlated with decreased risk of different kind of cancer; vitamin D synthesis is the only mechanism suggested to explain the effect of UVB irradiance on reducing cancer risk [26]. Results obtained in observational studies showed that if serum 25(OH)D levels were increased from a mean value of about 54 nmol/L to 110 nmol/L, life expectancies can be enlarged by two years [29].

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4. Vitamin D in dairy products

Dairy cows breeding started around 5,000 years ago during the late Neolithic and early Bronze Age in northern and central Europe [30]; dairy foods, that could be stored for long times in cold weathers, provided calories for human populations without worries related to the seasons or influenced by bad harvests. Moreover, milk helped, particularly in the north, to avoid diseases such as rickets, because of the relatively high concentration of vitamin D; natural synthesis of vitamin D in humans occurs only with sun-light exposition, so it is hard for people living in northern Europe to produce enough vitamin D during winter months.

Milk is a complete food providing several nutrients to the consumers, specifically carbohydrates (mainly lactose), proteins, fat, minerals and vitamins, contributing in an average human diet a mean daily intake of 134 kcal, 8 g of proteins and 7.3 g of fat [31]. Water is the most represented compound in all different kind of milks, ranging from water content lower than 50 percent in whale milk to a content close to 90 percent in donkey milk [32]. Dietary intake of vitamin D through milk has been investigated since the 1960s, when interesting contents of vitamin D were determined in cow's milk [1]. Some years later, sincerely, several experiments demonstrated that cow and human milk are not valid sources of this molecule; in fact, vitamin D content in cow's milk was determined in the range of 0.125–1 g/L [33]. In the same milk was found a vitamin D activity of 240 IU per liter, 85% of which is water soluble, attributed to vitamin D3-sulphate [34]. Other studies got to the conclusion that the biological activity of vitamin D3-sulphate is not high, with a very low contribution to the total vitamin D activity, determining a total content of vitamin D ranging between 5-35 IU/L [1]. Total amount of Vitamin D content can be described using different units, such as micrograms (μg) or International Units (IU); the most common unit used in Europe to describe vitamin D content is represented by μg, while to convert μg to IU the content in μg must be multiplied by 40 [35].

Human milk contains 24,25-dihydroxycholecalciferol and 1,25-dihydroxy vitamin D3, these two molecules represent about 15% of vitamin D activity [34]; vitamin D content in human milk is considered very low. A study performed on 198 children, followed up to 9 years of age, evaluated the effect of maternal vitamin D status during pregnancy on childhood skeletal growth [9]. Results obtained in the children 9 years old fed by mothers who had vitamin D insufficiency (25 OHD levels < 40 nmol/L, 31%, n = 49) or vitamin D deficiency (25 OHD levels < 25 nmol/L, 18%, n = 28) during late pregnancy showed a lower whole body and lumbar spine bone mineral content (BMC). According to the results of this study, vitamin D supplementation is recommended in pregnant women, particularly during the winter months, in order to obtain a long-lasting positive effect on peak bone mass (PBM) attainment and a reduced risk of osteoporotic fracture in elderly age [36].

A recent study [37] determined a very interesting total vitamin D content in donkey milk (23 mg/L, about 920 IU/L), higher compared to the values obtained analyzing milk produced by several mammalian species, including human milk [2]. Even if donkey milk represents a niche product, the importance of this interesting result is correlated to its use in special categories of consumers at risk of nutritional deficiencies, such as children and/or elderly; in these patients, donkey milk could help in avoiding lack of vitamin D [38].

Recently milk consumption is decreased, consequently dietary intake of vitamin D drinking fresh milk has declined, while cheese consumption has significantly increased by almost 100% since 1980 [39]. The large growth of human population and the change in food consumption habits created the right condition for producing new fortified foods able to provide the recommended intake of vitamin D in the daily diet. Milk does not provide the dietary requirements of vitamin D (Table 3), while cheese can represent the right food for the recommended dietary intake of this nutrient; in the States the fortification level of vitamin D in cheese is strictly regulated by the U.S. Food and Drug Administration [39].

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Table 3. Natural vitamin D content (μg/100 g) in foods.

Foodstuff	Vitamin D
Whole milk	0.1
Cheese, cheddar	0.3-0.6
Yogurt	0.1
Butter	1.5
Egg yolk	4.9-5.4
Mushrooms, chanterelle	5.3-14.2
Cod liver oil	210-250
Salmon, wild	13.1-24.7
Salmon, farmed	6.0
Herring	5.7-15.4
Cod	Trace-2.6
Sole	Trace-2.8

Source: modified by O'Mahoney et al. [35].

5. Fortified Foods

A diet based on the use of a few foods in which intake of animal source foods is poor can be characterized by a lack of micronutrients. In some areas of the world, especially in developing countries, diets may have sufficient energy level, while micronutrients intake is often not enough compared with dietary requirements. Food companies use a large amount of salt, sugar, vegetable fats and refined cereals to produce long life foods, all of which are characterized by the low vitamins and minerals content [40]. A diet based mainly on this kind of industrial foods normally does not cover the daily dietary requirement of several micronutrients, including vitamin D (Table 4). Lack of micronutrients is a widespread problem all over the world, creating both health and financial consequences in poor countries, because this lack can be the cause of infectious and parasitic diseases, causing a decrease of nutrient absorption and their biological utilization. The attention of clinicians and nutritionists in the past years was targeted firstly to get proteins sufficiency, later to provide energy sufficiency and actually is aimed to obtain micronutrients sufficiency.

Table 4. Prevalence of Vitamin D deficiency (25-OH-D3 < 50 nmol/L) in Southeast Asia.

Country	Age (yers)	Prevalence (%)
Vietnam	Childbearing age	7
Indonesia	18-40	63
Thailand	15-98	5.7
Malaysia	7-12	72.4
Malaysia	48-53	41 males, 87 females

Source: modified by Yang et al. [41].

An easy and practical method to avoid micronutrients deficiency is represented by fortification of commonly consumed staple foods [42]. The first case of food fortified dated around 4000 years BC,

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when the Persian physician Melampus enriched wine with iron filings to increase the sailors' resistance and their sexual activity [43]. Around six thousand years later, in 1833, in France the chemist Boussingault inserted iodine into salt to prevent goiter; later, during 1920s in Denmark vitamin A was put in margarine, while during 1930s in the United States, in order to prevent rickets in children, dairy companies started to add vitamin D to milk [44].

In the human body, ingested vitamin D2 and endogenously produced vitamin D3 are converted to the biologically active form, 1,25-dihydroxyvitamin D [1,25(OH)2D], named calcitriol. In 1969 was detected the nuclear vitamin D receptor (VDR) for 1,25(OH)2D, that till today has been determined in at least 38 human tissues and organs [35]. In fact, VDR has been firstly detected in the bone, kidney and gastrointestinal tract; later has been found in several other tissues, including those in the brain, breast, colon and prostate. The phosphoprotein VDR is involved in different biological functions of calcitriol; because of its widespread distribution, Vitamin D is not considered as just a calcaemic hormone, and vitamin D deficiency is now implicated in a series of different other diseases such as psoriasis, multiple sclerosis, inflammatory bowel disease, type 1 and type 2 diabetes, hypertension, cardiovascular disease, the metabolic syndrome and various cancers [35].

The optimal vitamin D status has not been yet determined; the Endocrine Society's Clinical Practice Guidelines established the lower serum threshold for 25(OH)D level as 75 nM or 30 ng/mL [45]. The Institute of Medicine (IOM) recommended intake (600 IU/day) for people in the range of age between 1–70 years is not enough to get to the required level (≥30 ng/mL) above mentioned [46]. Using supplements and/or fortified foods it is possible to receive an extra intake of 1000–4000 IU/day of vitamin D that is considered a necessary daily dose, together with dietary intake and endogenous production [46].

6. Vitamin D Fortification Strategies

Milk fortification with vitamin D started in the USA during the 1930s [47]. At the beginning milk was fortified by irradiating milk with vitamin D or, as an alternative, by feeding the cows using irradiated yeast. During the 1940s was developed a new simple and valid method based on vitamin D concentrate direct addition to milk; this practice is still used today. Vitamin D fortification of foods is voluntary in the States, and it is strictly regulated considering each different food category, the use and the recommended daily intake, fulfilling the aim of avoiding over-fortification. Strangely, vitamin D is supplemented to most of the fresh milk sold in the United States, but it is not added to other dairy products, even if it is permitted to fortify cheese and cheese products. Vitamin D is also supplemented to breakfast cereals, soy and rice beverages, and orange juice, usually together with calcium. In Canada it is permitted to fortify adding vitamin D to milk (180 IU/250 mL) and margarine (530 IU/100 g); as in the USA, vitamin D fortification is voluntary, but the fortification dose to add is always clearly described [40].

In the States, several RTE (ready-to-eat) breakfast cereals are fortified with vitamin D, that it is also added in some yogurt and margarines, while in Canada it is not permitted to fortify RTE breakfast cereals; However, in permitted foods, fortification of vitamin D must not exceed 20 IU/100 Calories [48]. The efficacy of vitamin D food fortification to increase vitamin D serum level has been tested [47]. Foods fortified with vitamin D normally contain 100 IU per serving; considering specifically milk fortified with vitamin D, its consumption increased vitamin D intake and was responsible for a significant increase of 25(OH)D levels [35]. An average daily intake of about 11 μg (440 IU/day) using fortified foods (range 120–1000 IU/day) achieved 25(OH)D concentrations to 7.7 ng/mL. This corresponded to a 0.5 ng/mL daily increase in 25(OH)D for each 40 IU (1 μg) ingested [47]. The most common food fortified with vitamin D is milk, contributing 44% of total daily vitamin D intake. Teen-agers males (13 to 18 years) [49] had the highest vitamin D intakes among the age/sex categories, but for all the consumers considered in that study dietary requirement level of 400 IU in order to reach serum levels of 16 ng/mL was not enough [50]. Therefore, considering the vitamin D dietary requirement covered when in serum vitamin D level is ≥30 ng/mL, the actual consumers mean intake of vitamin D can be considered low and not adequate compared to the daily nutritional requirements. Higher levels of vitamin D fortification are required in order to increase the number of

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consumers with serum levels of 25(OH)D ≥ 20 ng/mL. Vitamin D fortification strategies have also been evaluated in consumers living in developing countries, using fresh milk, cheeses and margarine, fortifying foods with both vitamins D and A, but results obtained in these programs have not been clearly discussed [51].

7. Vitamin D supplementation to prevent osteoporosis

The deposition of bone minerals starts during pregnancy, particularly in the last 90 days. Bone mass can increase about 40 times from birth to adulthood, with a peak close to 90% occurring close to the age ranging between 18 and 20 years; in fact, the most critical periods for bone minerals deposition are represented by childhood and adolescence [52].

In postmenopausal women, several studies based on vitamin D and Calcium supplementation have been performed, in order to determine the best nutritional strategies [15]. The preliminary data necessary for these clinical trials were represented by the threshold intakes of vitamin D and calcium below which skeletal health is compromised. Considering vitamin D, several clinical trials found a relationship between low levels of 25-hydroxyvitamin D (25[OH]D) and increased secretion of parathyroid hormone (PTH) which is responsible for bone loss in the elderly through increased bone resorption [15]. The serum content of 25(OH)D necessary to maintain adequate levels of PTH is considered ranging between 30 and 100 nmol/L [53]. Because of this great variability, vitamin D insufficiency within populations can be differently evaluated depending on the threshold used. In a study performed using 8532 postmenopausal, osteoporotic European women, 79.6% were considered to have inadequate level of vitamin D if the serum 25(OH)D threshold was fixed to the value of 80 nmol/L, while when the threshold was reduced to 50 nmol/L the women with severe lack of vitamin D were a smaller amount, 32.1 % [24]. Basing on the results obtained in several clinical trials, actually 80 nmol/L is considered to be an overestimate threshold while 50 nmol/L is believed to be an acceptable threshold [15].

Dose used for vitamin D supplementation must be enough to reach the threshold values of serum 25(OH)D, otherwise any desired target will be obtained. Clinical trials performed with the aim of determining the anti-fracture efficacy of different doses of vitamin D found that 400 IU per day was not enough to achieve a significant effect in reducing fracture rate [54]. Oral daily doses of 700–800 IU or 100,000 IU taken quarterly both showed a positive antifracture effect, while an annual intramuscular dose of 300,000 IU did not show valid efficacy [54]. The results obtained in these studies show that the most effective vitamin D supplementation in osteoporotic patients is obtained when administered orally either daily or quarterly; in case of a daily supplementation, the dose should be higher than 700–800 IU/day [55].

However, it is important to consider that, according to several clinical trials performed all over the world, the most effective anti-osteoporotic results have been achieved with combined treatment with calcium and vitamin D supplementation [17, 56]. Lack of vitamin D showed a decrease in the response to some treatments for osteoporosis, while the effects of antiosteoporotic treatments with calcium alone or vitamin D alone has never been properly described. In women over 65 year of age, risk of osteoporotic fracture can be frequent, particularly if a lack of calcium and/or vitamin D is associated. In these cases, calcium and vitamin D supplementation can be useful, administering doses respectively of 1000–1200 mg calcium and 800 IU vitamin D daily. The best recommended strategy is combining vitamin D and calcium into a unique supplement, in order to increase patient healthy status, with a consequent improvement of the treatment's efficacy.

8.Conclusions

Vitamin D plays an important role in controlling calcium and phosphate metabolism, contributing both in the formation of bones and in the bone health; the function of this vitamin in the human metabolism has been discovered since more than a century ago. Even if vitamin D is synthesized by the skin, dietary supplements are considered necessary for a healthy diet for some

categories of consumers, such as elderly women. Milk is the most common fortified food for human consumption. Use of fortified foods in children can prevent rickets, while in adults can be used in people not sufficiently exposed to sunlight. Risk of osteoporotic fracture is increased in case of vitamin D deficiency; an effective program of osteoporosis prevention is absolutely necessary, considering that by 2030, one in four of the human population, that means 25%, will be elderly. The most important target will be to meet all the dietary requirements, including micronutrients, for the improvement of bone health throughout the entire life cycle. Bone health in the actual younger population must be considered the target in the next years, too, developing new nutritional strategies.

Large doses of vitamin D can cause an increase in the calcium content in the blood that can damage the kidneys creating calcification of soft tissues (kidney stones). Recent studies suggest that excessive intake of vitamin D above dietary recommendations may be responsible for other health outcomes, such as a significant risk reduction of some kind of cancer. Using appropriate feeding strategies in dairy cows, natural vitamin D content can be increased in dairy products, especially in fresh milk; further studies are necessary in this way, optimizing the total natural vitamin D contents in dairy products, considering that in several countries fortification of food is not always permitted as a common practice.

Conflicts of Interest: "The authors declare no conflict of interest."

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