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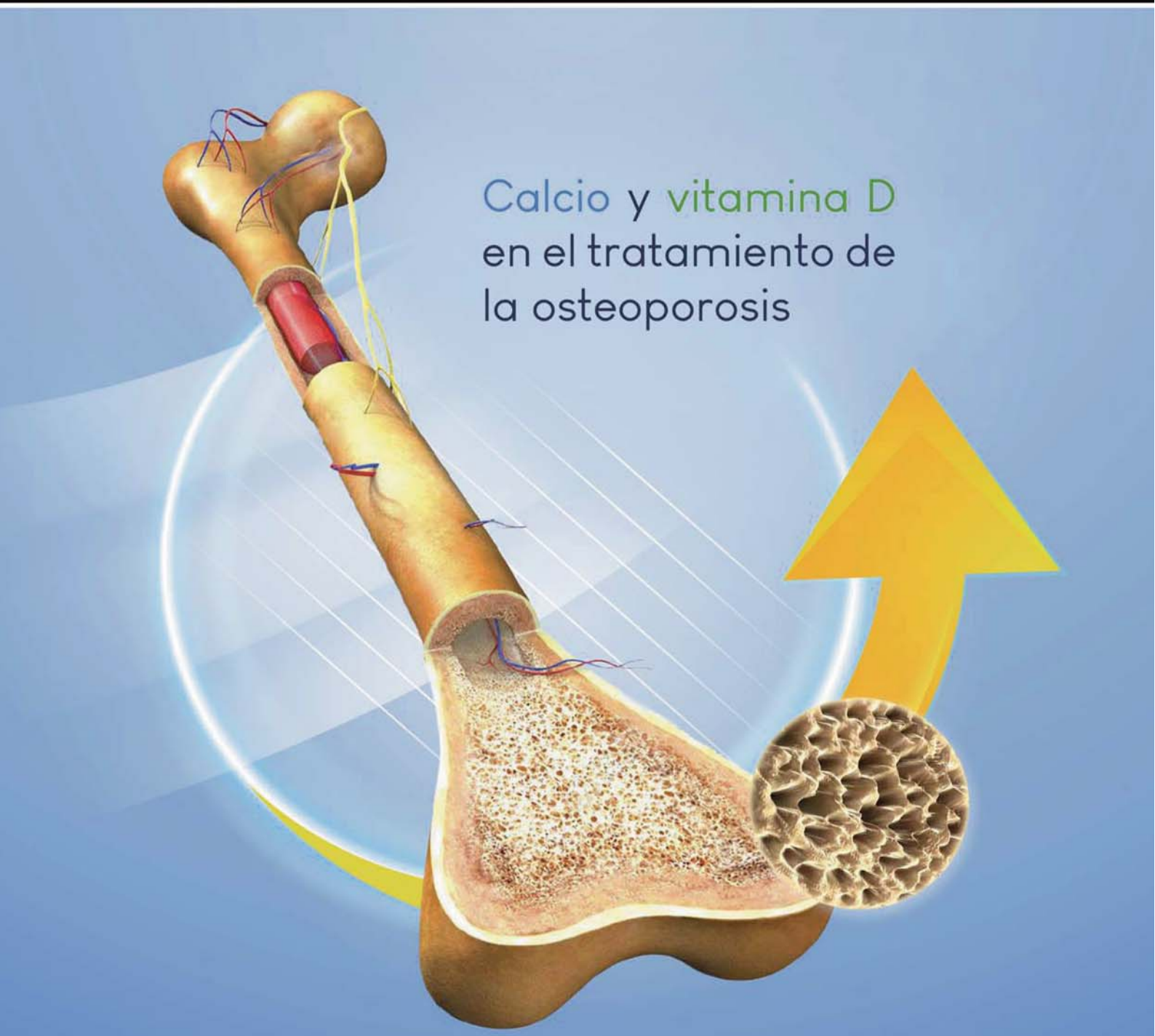

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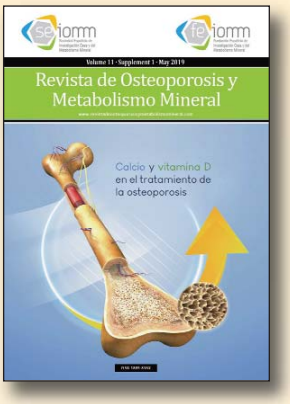

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Summary

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Myths, stories and legends about calcium and vitamin D

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Introduction

In recent years there has been an impressive increase in the number of scientific articles related to the metabolism of calcium and vitamin D. We have gained a much deeper knowledge of many patho-physiological aspects. However, and in spite of this, a series of fraudulence, myths and legends have been developed in parallel on both calcium and vitamin D, many of them absolutely unjustified, and others derived from a misunderstanding of some scientific articles. Since this can lead to the abandonment of treatments or taking them in the wrong way, we have developed this article in order to clarify, with scientific evidence, some of these aspects.

Review of the physiology of calcium and vitamin D

Calcium absorption depends on vitamin D and is a saturable mechanism. From a certain amount and reach the optimum level of absorption, all calcium that is ingested is not absorbed and is eliminated by feces.

Between 100 and 200 mg of calcium are removed by the kidney on a daily basis under normal conditions. Also, between 800 to 900 mg of calcium is lost by stool, as a result of the secretion of bile salts and pancreatic juices. These are known as "mandatory calcium losses" and together they constitute about 1,000 mg (Figure 1). Calcium cannot be synthesized by any metabolic route and, therefore, must be taken by diet[1].

Serum calcium levels must remain very stable, with hardly any oscillation between 8.8 and 10.5 mg/dl, because many of the physiological functions vital to the body, such as muscle contraction, nerve transmission, depend on the stability of these figures. and coagulation, just to name a few of them[1].

If daily losses are not replaced by intake, a negative balance is produced daily and, to maintain stable serum calcium levels, parathormone (PTH) is activated, which increases bone resorption and normalizes calcemia. If these circumstances are prolonged, in the long term, calcium-poor diets increase the risk of osteoporosis and fragility fractures[2,3].

"Humans do not need to drink milk after weaning"

False. Calcium is a mineral that cannot be synthesized by the body. Therefore, it must be ingested. But calcium is present mostly in dairy products, being difficult to reach the required daily amounts with other foods that are not dairy. Table 1 shows a relationship of the calcium content of the main foods, and table 2 shows the daily requirements established by consensus, depending on the different stages of life[4]. By taking 2 daily yogurts and 2 glasses of milk, we would fulfill these requirements.

If we avoid dairy products and eliminate them completely from the diet, a daily negative calcium balance would develop, since the obligatory losses are maintained, regardless of diet. The body cannot allow serum calcium levels to decrease. With a decrease in calcium intake, there is an increase in PTH, which increases bone resorption to avoid hypocalcemia. If this situation persists over a long period of time, a long-term loss of bone mass may occur, which will lead to osteoporosis and increased risk of fragility fractures[5].

On the other hand, populations with balanced diets rich in calcium, or with an intake of calcium supplements with or without vitamin D, reportedly present an increase in bone mineral density (BMD)[6] and a decrease in the risk of fracture[7], as well as a decrease in the risk of renal lithiasis[5].

Animals do not take dairy simply because they have not been able to domesticate other animals.

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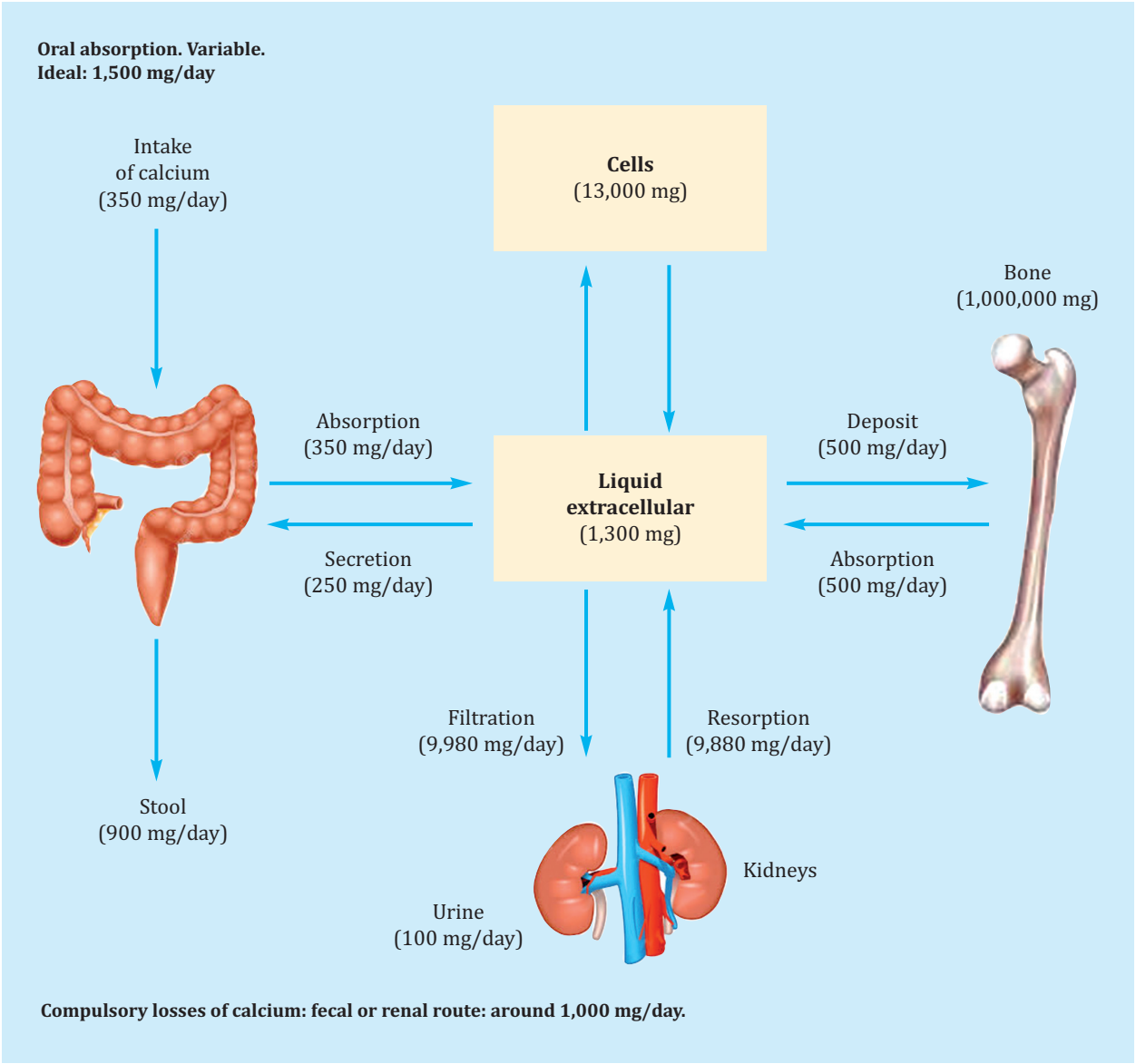
Figure 1. Physiology of calcium absorption and excretion



Compulsory losses of calcium: fecal or renal route: around 1,000 mg/day.

"Calcium with or without vitamin D should be taken with dinner or on an empty stomach"

There is no objective reason to justify this assertion. The most frequently used calcium salt is calcium carbonate, which is best absorbed in acidic media[8]. Therefore, calcium should be taken at the time when there is more acid in the stomach, which is just after lunch. As in our culture the most important meal is made at noon, it is after lunch when calcium should be taken. In the Anglo-Saxon culture, where people generally have a lighter lunch and a more abundant dinner, calcium should be taken after dinner, but always at the end of it.

Other salts such as citrate or calcium pidolate are better absorbed than carbonate, but are more expensive and, therefore, much less used. There is no reason to indicate fasting calcium intake and even less so that it is at night.

"Dairy intake (by diet or through supplements) increases the risk of lithiasis and ischemic heart disease"

It is a mistake to think that the calcium ingested by the diet or by supplements is immediately eliminated by the kidney, and that in the case of taking an excess of this mineral an increase in the risk of lithiasis is observed. All calcium kinetics are strictly regulated by the hormones involved in it: PTH, calcitonin and vitamin D itself, in addition to the kinetics itself that regulates the intra and extracellular flow of calcium.

We should take into account It should be taken into account what is indicated in the second section: a diet low in calcium causes the stimulation of PTH and this increases the urinary excretion of calcium[2]. Conversely, in patients with hypercalciuria, calcium and vitamin D supplementation produced a decrease in calciuria[5] and a decrease in recurrence of renal colic[9,10].

Table 1. Calcium content: milligrams per 100 g of edible portion of the product

Foods	Calcium content
Cured manchego cheese	1,200
Gruyere cheeses, emmental, roquefort	560 – 850
Fresh manchego cheese	470
Sardines in oil	400
Almonds, hazelnuts	240
Crayfish, prawns, prawns...	220
Burgos' cheese	186
Yogurt	127 – 180
Dried figs	180
Ice creams	150
Chickpeas	145
Custard and flan	140
Pistachios	136
Cow milk	130
White beans, dried beans	130
Clams, cockles, chirlas...	120
Milk chocolate	120
Milkshakes	120
Chard, thistle, spinach, leek...	87 – 114
Cheese in portions	98
Nuts, dates, raisins...	70
Olives	63
Cottage cheese and curd	60
Lobster and lobster	60
Lentils	56
Chicken egg	51
Cod	51
Cakes, pasta...	48
Sardines	43
Artichokes, cabbage, cabbage, green beans...	40

Table 2. Recommended daily amounts of calcium according to age. (National Institutes of Health, NIH)[4]

Stage of life	Recommended amount
Babies up to 6 months	400 mg
Babies between 6 months and 1 year	600 mg
Children 1-5 years	800 mg
Children from 6 to 10 years old	800 – 1,200 mg
Adolescents and young adults from 11 to 24 years old	1,200 – 1,500 mg
Women from 25 to 50 years old	1,000 mg
Pregnant or breastfeeding women	1,200 – 1,500 mg
Postmenopausal women with estrogenic therapy	1,000 mg
Postmenopausal women without estrogen therapy	1,500 mg
Men from 25 to 65 years old	1,000 mg
Men and women over 65	1,500 mg

In the same way, the ingested calcium will not be deposited directly in the arteries increasing the risk of arteriosclerosis and, underlying, the risk of ischemic heart disease. Some authors have suggested that the use of calcium supplements causes an increased risk of ischemic heart disease, myocardial infarction and sudden death[11-13]. These very alarming studies have had a great impact on the scientific community, are methodologically debatable, since they are mostly meta-analysis. In some of them, the diagnosis of myocardial infarction was self-reported, without medical reports[13]. Almost immediately, other meta-analyzes published opposite results. With the data we have today, it should not be feared that calcium supplements, with or without vitamin D, increase the risk of lithiasis or ischemic heart disease[14-18].

"In Spain there is no vitamin D deficit as it is a very sunny country"

This is one of the biggest myths. Spain is a world-class tourist destination, especially for its sun. So it is mistakenly thought that we enjoy that sun year round and, the most important mistake, that we take advantage of it properly.

In the first place, the country's location on the Earth, oblique with respect to its axis, means that we can only properly take in the sun's rays during the summer months. Outside this season, above the 35th parallel the sun's rays do not reach earth properly and almost all of Spain is above that parallel[19], with the exception of the Canary Islands.

Another circumstance that impedes the population from not taking advantage of the hours of sunshine is our lifestyle. We spend most of our life indoors. When we go out we do so fully dressed. In the sunnier months, because of the high temperatures we avoid going out. A fear of skin cancer means what little sun exposure we have is done with sunscreen, which minimizes vitamin D synthesis.

Thus there is a reported vitamin D deficiency in Spain similar to that of other European countries, both in healthy pre- or postmenopausal women[20], as well as in those with osteoporosis[21], and much more if they are isolated in chronic centers[22]. In Nordic countries, where they are aware of this problem, supplemented foods are available with vitamin D[23]. Thus, serum levels of the vitamin D or 25 (OH) vitamin D (25(OH)D) reserve are curiously lower in Spain, a "sunny par excellence" country than in the Nordic region. This has been called the "vitamin D paradox"[24].

Just to offer one example, the medical students of the University of Las Palmas de Gran Canaria, would be ideal candidates to present optimal levels of vitamin D: they are healthy, young, informed about the physiology of vitamin D and with all the hours of sunshine available. However, not taking advantage of these hours (they spend most of their time inside hospitals, classrooms and libraries), an insufficiency was reported –figures below 30 ng/ml of 25(OH)D– in 61% of them[25]. Similar results were found in elite athletes in Spain[26].

Table 3. Vitamin D metabolites

Metabolite	Name	Utility	Tradename
D3	Calciferol	Substratum	Cadelius D
25(OH)D	Calcidiol	Measure the reservation	Hidroferol
1,25(OH)2D	Calcitriol	Active principle	Rocaltrol

"All vitamins D are the same"

The skin synthesizes the first metabolite of vitamin D, which is the substrate, called calciferol. This is transported by a transport protein, the DBP (vitamin D binding protein) to the liver, where hydroxylation occurs, synthesizing calcidiol, which is an ideal metabolite to measure the body's vitamin D pool. Calcidiol is much more active than calciferol. These drugs are equally effective for us[27].

Finally, with the same transporter protein, 1 alpha hydroxylation is produced in the kidney, the final result being 1.25 dihydroxycholecalciferol or calcitriol, the biologically active metabolite (actually a hormone), which is what binds to the receptors of vitamin D (VDR) in virtually all body tissues[28].

To estimate serum vitamin D levels, the ideal metabolite is calcidiol[29]. However, for the therapeutic use of vitamin D supplements, the metabolite of choice is calciferol, for two reasons: first, it is the safest, since being at the beginning of the physiological chain, the body is able to direct the same towards the production of more or less active metabolites, since it has many reserve metabolites. Second, all the studies carried out in the field of osteoporosis with the reference drugs have been with calciferol[30].

Calcidiol should be reserved for patients suffering from liver failure and in cases of severe vitamin D deficiency, to obtain a rapid recovery from normal levels. However, given its potency, cases of hypercalcemia have been described with its use[31], and recently the Spanish Agency for Medicines and Health Products (AEMPS) has published a warning about several cases of poisoning with this drug[32].

Finally there is calcitriol, the active metabolite and, therefore, the hormone as such[33]. With its use, serum calcium levels should be monitored due to the risk of hypercalcemia. It is a potentially dangerous drug and, therefore, its dispensation is regulated by an inspection visa (see table 3).

Conflict of interests: The authors declare no conflict of interest.

Bibliography

1. Nordin BEC. Calcium homeostasis. Clin Biochem. 1990;23(1):3-10.
2. Quesada Gómez JM, Sosa Henríquez M. Nutrición y osteoporosis: calcio y vitamina D. Rev Osteoporos Metab Miner. 2011;3(4):165-82.
3. Recker RR, Cannata-Andía JB, Del Pino Montes J, Díaz-Curiel M, Nogués-Solán X, Valdés-Llorca C, et al. Papel del calcio y la vitamina D en el tratamiento de la osteoporosis. Rev Osteoporos Metab Miner. 2010;2(1):61-72.
4. No authors listed. Optimal calcium intake. NIH Consens Statement. 1994;12 (4):1-31.
5. Pfeffer MA, Braunwald E, Moyé LA, Basta L, Brown EJ, Cuddy TE, et al. A prospective study of dietary calcium and other nutrients and the risk of symptomatic kidney stones. N Engl J Med. 1993;327(10):669-77.
6. O´Brien KO. Combined calcium and Vitamin D supplementation reduce bone loss and fracture incidence in older men and women. Nutr Rev. 1998;56 (5):148-50.
7. Beto J. The role of calcium in human aging. Clin Nutr Res. 2015;4:1-8.
8. Booth A, Camacho P. A closer look at calcium absorption and the benefits and risks of dietary versus supplemental calcium. Postgrad Med. 2013; 125(6):73-81.
9. Ganji MR. Postmenopausal osteoporosis treatment and risk of urinary calculus development. Iran J Kidney Dis. 2013;7(3):171.
10. Haghighi A, Samimagham H, Gahardehi G. Calcium and vitamin D supplementation and risk of kidney stone formation in postmenopausal women. Iran J Kidney Dis. 2013;7(3):210-3.
11. Reid IR, Bolland MJ, Avenell A, Grey A. Cardiovascular effects of calcium supplementation. Osteoporos Int. 2011; 22(6):1649-58.
12. Bolland MJ, Grey A, Avenell A, Gamble GD, Reid IR. Calcium supplements with or without vitamin D and risk of cardiovascular events: Reanalysis of the Women's Health Initiative limited access dataset and meta-analysis. BMJ. 2011;342:d2040.
13. Bolland MJ, Barber PA, Doughty RN, Mason B, Horne A, Ames R, et al. Vascular events in healthy older women receiving calcium supplementation: Randomised controlled trial. BMJ. 2008;336(7638):262-6.
14. Bostick RB, Kushi LH, Wu Y, Meyer KA, Sellers TA, Folsom AR: Relation of calcium, vitamin D, and dairy food intake to ischemic heart disease mortality among postmenopausal women. Am J Epidemiol. 1999;149(2):151-61.
15. Lewis JR, Calver J, Zhu K, Flicker L, Prince RL. Calcium supplementation and the risks of atherosclerotic vascular disease in older women: Results of a 5-year RCT and a 4.5-year follow-up. J Bone Miner Res. 2011;26(1):35-41.
16. Korownyk C, Ivers N, Allan GM. Does calcium supplementation increase risk of myocardial infarction? Can Fam Physician. 2011;57(7):798.
17. Sabbagh Z, Vatanparast H. Is calcium supplementation a risk factor for cardiovascular diseases in older women? Nutr Rev. 2009;67(2):105-8.
18. Al-Delaimy WK, Rimm E, Willett WC, Stampfer MJ, Hu FB. A prospective study of calcium intake from diet and supplements and risk of ischemic heart disease among men. Am J Clin Nutr. 2003;77(4):814-8.
19. Serrano MA, Cañada J, Moreno JC, Gurrea G. Solar ultraviolet doses and vitamin D in a northern mid-latitude. Sci Total Environ. 2017;574:744-50.
20. González-Molero I, Morcillo S, Valdés S, Pérez-Valero V, Botas P, Delgado E, et al. Vitamin D deficiency in Spain: A population-based cohort study. Eur J Clin Nutr. 2011;65(3):321-8.
21. Hernández JL, Olmos JM, Pariente E, Nan D, Martínez J, Llorca J, et al. Influence of Vitamin D status on vertebral fractures, bone mineral density, and bone turnover markers in normocalcemic postmenopausal women with high parathyroid hormone levels. J Clin Endocrinol Metab. 2013;98(4):1711-7.
22. Rodríguez Sangrador M, Beltrán De Miguel B, Quintanilla Murillas L, Cuadrado Vives C, Moreiras Tuny O. Contribución de la dieta y la exposición solar al estatus nutricional de vitamina D en españolas de edad avanzada; estudio de los cinco países (Proyecto OPTIFORD). Nutr Hosp. 2008;23(6):567-76.
23. Tenta R, Moschonis G, Koutsilieris M, Manios Y. Calcium and vitamin D supplementation through fortified dairy products counterbalances seasonal variations of bone metabolism indices: The Postmenopausal Health Study. Eur J Nutr. 2011;50(5):341-9.
24. Sorthe J, Moghaddam A. Lactase persistence may explain the paradoxical findings of high vitamin D concentrations in Europeans living in areas of low UV-B irradiation. Eur J Clin Nutr. 2019;73(4):585-93.
25. González-Padilla E, Soria López A, González-Rodríguez E, García-Santana S, Mirallave-Pescador A, del Val Groba Marco M, et al. High prevalence of hypovitaminosis D in medical students in Gran Canaria. Canary Islands (Spain). Endocrinol y Nutr. 2011;58(6):267-73.
26. Valtueña J, Dominguez D, Til L, González-Gross M, Drobnic F. Alta prevalencia de insuficiencia de vitamina D entre deportistas de élite españoles: la importancia de la adaptación del entrenam. Nutr Hosp. 2014;30(1):124-31.
27. Navarro-Valverde C, Sosa-Henríquez M, Alhambra-Expósito MR, Quesada-Gómez JM. Vitamin D3 and calcidiol are not equipotent. J Steroid Biochem Mol Biol. 2016;164:205-8.
28. Holick M. Vitamin D deficiency. N Engl J Med. 2007;357(3):266-81.
29. Glendenning P, Inderjeeth CA, Holick M. Measuring vitamin D. Clin Biochem. 2012;38(12):901-6.
30. Compston JE, McClung MR, Leslie WD. Osteoporosis. 2019;393:364-76.
31. Garcia Doladé N, Cereza García G, Madurga Sanz M. Riesgo de hipercalcemia e hipervitaminosis D por calcifediol. Revisión de casos notificados al Sistema Español de Farmacovigilancia. Med Clin (Barc). 2013;141(2):88-9.
32. Sanitarios AE de M y PS. Vitamina D: casos graves de hipercalcemia por sobredosificación en pacientes adultos y en pediatría. Agencia Española Medicam y Prod Sanit 2019;Marzo:1–6. Disponible en: https://www.aemps.gob.es/informa/notasInformativas/medicamentosUsoHumano/seguridad/2019/docs/NI_MUH_FV-2-2019-vitamina-D.pdf.
33. Norman AW. From vitamin D to hormone D: fundamentals of the vitamin D endocrine system essential for good health. Am J Clin Nutr. 2008;88(2):491s-9s.

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Self assessment test

1. The mandatory calcium losses are:

a. Through the skin, and breathing, about 250 mg daily
b. By stool and breathing, about 500 mg daily
c. In urine, about 400 mg daily
d. Urine and feces, about 1,000 mg daily

2. A woman after menopause is advised to take daily:

a. 250 mg of calcium
b. 500 mg of calcium
c. 1,000 mg of calcium
d. 1,500 mg of calcium

3. The Spanish paradox of vitamin D indicates:

a. That vitamin D is not what it seems to be
b. That vitamin D levels are normal in Spain
c. That vitamin D levels are low in the Nordic countries
d. All of the above is false

4. Which of the following foods has a higher calcium content in milligrams per 100 g of edible portion:

a. Olives
b. Sardines
c. Chicken eggs
d. Cured Manchego cheese

5. What is the prevalence of hypovitaminosis D in medical students of the University of Las Palmas de Gran Canaria? (25HCC values below 30 ng/mL):

a. 15%
b. 25%
c. 40%
d. 61%

Correct answers can be found on pages 23 and 24

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Recommendations of scientific societies on calcium and vitamin D supplementation in osteoporosis

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Introduction

Calcium and vitamin D requirements for health in general and bone in particular are well established. While the medical community recommends maintaining serum levels of 25 hydroxy-vitamin D (25(OH)D) above at least 20 ng/ml, the calcemia should remain between 8.5 and 10.5 mg/dl. However, these amounts, which should be obtained naturally from diet (calcium) and sun exposure (vitamin D), are not attained by a high percentage of the population.

Calcium levels, so essential for the operation of multiple systems, are maintained thanks to the store that constitutes the bone. From this, the body obtains calcium to maintain its homeostasis if necessary, to the detriment, obviously, of the bone itself, which undergoes an increased resorption that, in turn, produces osteoporosis.

Vitamin D, for its part, lacking a storage system, sees its serum levels fall as sun exposure decreases. We know that the foods richest in calcium are dairy. The intake of these foods is very low in the general population, for different reasons. Furthermore, the risk of skin cancer causes sun exposure to be avoided "drastically", which prevents vitamin D production. Calcium and vitamin D supplements help people reach the appropriate levels in these situations and shore up deficiencies.

In this paper, we will discuss the recommendations made in various clinical guidelines. These are selective, given the limited space, but we believe they are representative and shed light on the usefulness of giving calcium and vitamin D supplements for the treatment of osteoporosis or to ensure bone health . The approach that different societies and institutions have made varies from the one carried out in the framework of the general treatment of osteoporosis to the specific one of such supplements, either only of vitamin D, of calcium alone, or of both.

The Spanish Society of Bone Research and Mineral Metabolism (SEIOMM)

In the 2014 update of its clinical practice guidelines in postmenopausal, glucocorticoid and male osteoporosis of 2008[1,2], the SEIOMM concludes that there are doubts regarding the efficacy of calcium or vitamin D given alone for the treatment of osteoporosis. They point out that "administered together they seem to have a certain degree of efficacy in preventing non-vertebral fractures, which is clearer in people with deficits in them, such as the case of elderly people living in residences. There is virtually no evidence of its effectiveness in preventing vertebral fractures. Regardless of the above, which refers to people not selected for osteoporosis, there is universal consensus that patients with this disease should receive calcium and vitamin D along with the main treatment of the disease." The recommended contribution is 1,000-1,200 mg/day of calcium and 800 IU/day of vitamin D, so if these figures are not reached with the diet, supplements should be added.

In 2011, a panel of experts from various Spanish scientific societies led by SEIOMM formulated a position paper on the needs and optimal levels of vitamin D[3]. In their recommendations, the optimal serum levels of vitamin D was considered to be between 30 and 75 ng/ml, and that levels below 20 ng/ml are clearly pathological. Regarding vitamin D requirements, it was recommended that for postmenopausal women they should be 600-800 IU/day, while in the elderly, patients with osteoporosis, fractured patients and patients receiving glucocorticoids the amounts should rise to 800-1,000 IU/day.

Based on the high prevalence of severe vitamin D deficiency in patients with osteoporotic hip fracture, the panel deemed it advisable to make a determination of vitamin D levels, and when not possible, the use of higher doses.

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Focusing on the prevention of osteoporosis, it is pointed out that it must be carried out with good hygienic-dietary habits (adequate sun exposure, calcium-rich diet), and that the use of calcium and vitamin D supplements for this purpose is not indicated, except in cases where there is a situation that makes it difficult to obtain the optimum levels of these substances, which will be supplemented pharmacologically.

Regarding the treatment of osteoporosis, it is pointed out that there is no evidence that the exclusive treatment of calcium and vitamin D has anti-fracture efficacy, except in a certain population, such as the institutionalized elderly. However, they do consider it necessary to add vitamin D and calcium supplements together with other anti-osteoporotic drugs, although in those patients in whom adequate calcium intake is guaranteed through diet, it is not necessary to use supplements of this element.

Spanish Society of Endocrinology and Nutrition (SEEN)

In 2017, SEEN published a consensus document on vitamin D recommendations for the general population[4], and regarding treatment with vitamin D supplements suggests:

- Use vitamin D3 (cholecalciferol) or 25(OH)D (calcifediol) to treat vitamin D deficiency.
- Calculate the required dose of vitamin D depending on the etiology and severity of the deficit, as well as the type of vitamin D that will be used to treat it.
- Monitor serum concentrations of 25(OH)D to assess the response to treatment at intervals every 3-4 months until adequate concentrations of 25(OH)D are reached, and then at intervals every 6 months.
- A vitamin D contribution of 800-1,000 IU/day in people over 65 and in institutionalized people to improve their bone health and reduce the risk of non-vertebral fracture.
- A contribution of vitamin D of at least 800 IU/day in adults over 50 years of age together with an adequate intake of calcium (1,000-1,200 mg/day) to improve bone health and reduce the risk of fractures.
- Not recommending systematic supplementation in all adults under 50 years of age to obtain improvement in bone health, given the lack of existing data.

On the other hand, regarding the effect on the incidence of falls from treatment with vitamin D supplements, it is recommended that patients with vitamin D deficiency and high risk of falls be treated with supplements.

American Association of Clinical Endocrinologists/ American College of Endocrinology

In its 2016 guidelines for the diagnosis and treatment of postmenopausal osteoporosis, the American Association of Clinical Endocrinologists and the American College of Endocrinology[5] include among its recommendations the following referring to calcium and vitamin D supplements:

- Give vitamin D supplements if necessary to maintain optimal serum levels of 25(OH)D, for which doses of 1,000 to 2,000 IU daily are needed as sustained therapy.
- Higher doses may be necessary in the presence of certain factors, such as obesity, malabsorption, transplant patients, certain ethnicities, or in the elderly.
- Patients should be advised to maintain an adequate calcium intake of 1,200 mg/day for women over 50, which if not achieved by diet should be supplemented with supplements.

National Osteoporosis Society (NOS) (United Kingdom)

Although these guidelines are not established for the treatment of osteoporosis, the National Osteoporosis Society developed them in 2014 as guidelines for the management of vitamin D deficiency in adult patients with or at risk of developing bone disease[6]. In them, serum levels of 25(OH)D below 10 ng/ml (30 nmol/l) are established as vitamin D deficiency, and, recognizing that there is no consensus on this, they do support the majority in favor of consider as inappropriate values those that are between 20 and 30 ng/ml (at least in some populations), considering that levels above 30 mg/ml are sufficient.

They indicate that routinely testing vitamin D may be unnecessary in patients with osteoporosis or fragility fracture, who may be prescribed vitamin D supplements with antiresorptive therapy. As for the treatment of vitamin D deficiency, they recommend cholecalciferol (vitamin D3) better than ergocalciferol (D2) (although the latter can be used), and if what is needed is a rapid correction of the deficiency (for example, in the event of symptomatic disease or treatment with a potent antiresorptive), the recommended doses are in an initial shock regimen to provide a total of 30,000 IU of vitamin D (distributed in weekly or daily doses for 6-10 weeks); to continue with a maintenance regime consisting of doses of 800-2,000 IU daily (occasionally above 4,000 IU), given both daily and intermittently at higher doses. When the correction is less urgent, and when vitamin D supplements are prescribed with oral antiresorptive agents, the previous maintenance therapy can be performed without specifying the previous shock.

The Endocrine Society

The Endocrine Society published in 2011 its guidelines for the assessment, treatment and prevention of vitamin D[7] deficiency. Its objective was similar to that marked 3 years later by the National Osteoporosis Society (NOS), which we have just discussed. They suggest that all adults over 50 require at least 600 IU (50 to 70 years) to 800 IU (>70 years) daily of vitamin D, although without knowing if these amounts are sufficient to provide all the benefits for musculoskeletal health associated with vitamin D; and that to raise blood levels of 25(OH)D above 30 ng/ml, at least 1,500-2,000 IU daily of vitamin D supplement may be

required. In this regard, they also recommend using vitamin D2 or D3. Finally, for the treatment of vitamin D deficiency in adults suggest doses of 50,000 IU once a week for 8 weeks, or its equivalent of 6,000 IU daily to reach levels of 25(OH)D above 30 ng/ml, following maintenance doses of 1,500-2,000 IU daily.

Other guides

Other guides and position documents have been made for the management of vitamin D in the general population or for the treatment of osteoporosis[8-13], but basically the recommendations coincide with those of the aforementioned guidelines, with slight variations that They depend on the population to which they are directed.

Conclusions

While it is generally accepted that calcium and vitamin D supplements have not proven themselves effective for treating osteoporosis or preventing fractures (except in institutionalized elderly), if it is accepted that it is necessary to maintain adequate levels of calcium and vitamin D in the population for bone health. Such levels can preferably be acquired naturally, through diet and sun exposure, but when these are not adequate, supplementation is necessary.

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Bibliography

1. González Macías J, Guañabens Gay N, Gómez Alonso C, del Río Barquero L, Muñoz Torres M, Delgado M, et al. Guías de práctica clínica en la osteoporosis posmenopáusica, glucocorticoidea y del varón. Sociedad Española de Investigación Ósea y del Metabolismo Mineral. Rev Clin Esp. 2008;208 (Sup 1):1-24.
2. González-Macías J, Del Pino-Montes J, Olmos JM, Nogués X; en nombre de la Comisión de Redacción de las Guías de Osteoporosis de la SEIOMM. Guías de práctica clínica en la osteoporosis postmenopáusica, glucocorticoidea y del varón. Sociedad Española de Investigación Ósea y del Metabolismo Mineral (3ª. versión actualizada 2014). Rev Clin Esp. 2015;215:515-26.
3. Gómez de Tejada Romero MJ, Sosa Henríquez M, Del Pino Montes J, Jódar Gimeno E, Quesada Gómez JM, Cancelo Hidalgo MJ, et al. Documento de posición sobre las necesidades y niveles óptimos de vitamina D. Rev Osteoporos Metab Miner. 2011;3(1):53-64.
4. Varsavskya M, Rozas Moreno P, Becerra Fernández A, Luque Fernández I, Quesada Gómez JM, Ávila Rubio V, et al. Recomendaciones de vitamina D para la población general. Documento de consenso del Grupo de Trabajo de Osteoporosis y Metabolismo Mineral de la Sociedad Española de Endocrinología y Nutrición. Endocrinol Diabetes Nutr. 2017;64(S1):7-14.
5. Camacho PM, Petak SM, Binkley N, Clarke BL, Harris ST, Hurley DL, et al. American Association of Clinical Endocrinologists and American College of Endocrinology: clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis 2016. Endocr Pract. 2016;22(Suppl 4):1-42.
6. Aspray TJ, Bowring C, Fraser W, Gittoes N, Javaid MK, Macdonald H, et al. National Osteoporosis Society vitamin D guideline summary. Age Ageing. 2014;43(5):592-5.
7. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2011;96(7):1911-30.
8. Cesareo R, Attanasio R, Caputo M, Castello R, Chiodini I, Falchetti A, et al. Italian Association of Clinical Endocrinologists (AME) and Italian Chapter of the American Association of Clinical Endocrinologists (AACE) position statement: clinical management of vitamin D deficiency in adults. Nutrients. 2018;27;10(5).
9. Qaseem A, Forciea MA, McLean RM, Denberg TD; Clinical Guidelines Committee of the American College of Physicians. Treatment of low bone density or osteoporosis to prevent fractures in men and women: a clinical practice guideline update from the American College of Physicians. Ann Intern Med. 2017;166(11):818-39.
10. Scottish Intercollegiate Guidelines Network (SIGN). Management of osteoporosis and the prevention of fragility fractures. A national clinical guideline. Edinburgh: SIGN; 2015. (SIGN publication no. 142). [March 2015]. Available from URL: http://www.sign.ac.uk.
11. Crandall M, Duncan T, Mallat A, Greene W, Violano P, Christmas AB, et al. Prevention of fall-related injuries in the elderly: An Eastern Association for the Surgery of Trauma practice management guideline. J Trauma Acute Care Surg. 2016;81(1):196-206.
12. The US Preventive Services Task Force (USPSTF). Vitamin D, calcium, or combined supplementation for the primary prevention of fractures in community-dwelling adults. US Preventive Services Task Force Recommendation Statement. JAMA. 2018; 319(15):1592-9.
13. Haq A, Wimalawansa SJ, Pludowski P, Anouti FA. Clinical practice guidelines for vitamin D in the United Arab Emirates. J Steroid Biochem Mol Biol. 2018;175:4-11.

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Self assessment test

1. For the National Osteoporosis Society (NOS) of the United Kingdom, vitamin D deficiency occurs when serum levels of 25 hydroxyvitamin D (25HCC) are lower than:

a. *30 ng/mL*
b. *25 ng/mL*
c. *20 ng/mL*
d. *10 ng/mL*

2. For the American Association of Clinical Endocrinologists/American College of Endocrinology, patients over 50 must maintain a daily calcium intake of at least:

a. *800 mg*
b. *1,000 mg*
c. *1,200 mg*
d. *1,500 mg*

3. For the Spanish Society of Bone Research and Mineral Metabolism, patients with osteoporosis should receive a daily intake of calcium and vitamin D from:

a. *800 mg of calcium and 400 IU of vitamin D*
b. *1,000 mg of calcium and 800 IU of vitamin D*
c. *1,200 mg of calcium and 400 IU of vitamin D*
d. *None of the above*

4. For the Endocrine Society, adults over 50 must reach some serum values of 25(OH)D greater than:

a. *30 ng/mL*
b. *25 ng/mL*
c. *20 ng/mL*
d. *10 ng/mL*

5. One of the following recommendations of the (SEEN) on vitamin D is false:

a. *The required dose of vitamin D should be calculated depending on the etiology and severity of the deficit.*
b. *You should monitor serum concentrations of 25(OH)D to assess the response to treatment at intervals every 3-4 months until adequate concentrations of 25(OH)D are reached, and then at intervals every 6 months*
c. *A vitamin D contribution of 800-1,000 IU/day in people over 65 and in institutionalized people to improve their bone health and reduce the risk of non-vertebral fracture*
d. *Systematic supplementation is recommended in all adults under 50 years of age to obtain bone health improvement*

Correct answers can be found on pages 23 and 24

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The role of calcium and vitamin D in the prevention and treatment of osteoporosis

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Introduction

The role of calcium and vitamin D in bone metabolism has been known for many years. Calcium is one of the main components of bone and, together with the collagen matrix, it is responsible for facilitating the strength and resistance of the skeleton[1].

The maximum bone mass is acquired by 30 years of age and depends on genetic and environmental factors, including calcium intake. Once the bone mass peak is achieved, it is necessary to maintain a minimum calcium intake to avoid bone loss.

Vitamin D is responsible for maintaining calcium and phosphorus homeostasis, favoring its reabsorption at the renal and intestinal levels. Its deficit is associated with an alteration of bone mineralization, causing rickets in children and osteomalacia in adults.

Osteoporosis is a prevalent chronic process. It poses a public health problem associated with significant morbidity and mortality[2]. With the aging of the population its prevalence is expected to increase[3]. Physical activity and proper nutrition are two measures associated with a reducted risk of osteoporosis[4]. Adequate calcium intake, together with sufficient levels of vitamin D, have proven to be a good option to maintain a healthy bone state[5].

Calcium, vitamin D and muscle function

The interaction between the skeleton and its associated musculature occurs through direct mechanical effect and potential hormonal mechanisms.

In this sense, calcium plays a very important role through the control and neuromuscular regulation of intracellular myosin fibers, responsible for the contraction and relaxation of skeletal muscle[6]. Vitamin D absorbs and regulates calcium in muscle cells[7].

There is limited evidence regarding the use of calcium and vitamin D supplements and the loss of muscle mass and the increase in falls associated with aging. A systematic review suggests a low but significant positive effect of supplementation on muscle strength, but not on muscle mass or power[8]. No differences were observed between the use of vitamin D supplements compared to vitamin D supplements with calcium.

Reduced muscle function is associated with an increased risk of falls and, consequently, an increased risk of osteoporotic fractures. Supplementation with 700-1,000 IU of vitamin D (alone or associated with calcium) is associated with a 19% decrease in the risk of falls[9]. The role of calcium is controversial, although recent data suggest that its addition or not to vitamin D does not affect the risk of falls[10,11].

Thus, although calcium is intimately involved in muscular physiology, the evidence suggests that optimization of vitamin D, instead of calcium supplementation, reduces the risk of falls[12].

Calcium, vitamin D and bone metabolism

Proper nutrition with a sufficient calcium intake is necessary to acquire correct peak bone mass towards the third decade of life. Beyond that era, bone mass begins to decrease progressively, steadily in men and accelerated in postmenopausal women. To curb the slope of bone loss, an adequate supply of calcium and optimal levels of vitamin D should be maintained.

In general, a daily calcium intake of 1,000 mg is considered appropriate in children until adolescence, at which time the calcium provided should be about 1,300 mg/day. Between the ages of 19 and 50, a contribution of 1,000 mg/day is recommended, which should increase to 1,200 mg/day in women after menopause and in men after the seventh decade of life. As for the vitamin D intake, it is recommended that it be between 600-800 IU/day[13].

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A recent meta-analysis observed a slight increase in bone mineral density (BMD) in relation to the increase in calcium intake, both through diet (0.6-1.8%) and supplements (0.7 -1.8%)[14].

As for vitamin D, it is responsible for the maintenance of calcium homeostasis. Very low levels are associated with the appearance of osteomalacia and high levels can increase bone resorption and deteriorate mineralization, so prudent use in normal clinical practice is recommended[15]. In addition, observed BMD change is related to the basal plasma levels of 25-OH vitamin D and changes in levels over time[16].

Therefore, the European Medicines Agency recommends an adequate supply of calcium (in the diet or through the use of supplements), as well as physical activity and adequate levels of vitamin D to maintain bone health[17].

Calcium and vitamin D in the treatment of osteoporosis

Most drugs approved for the treatment of osteoporosis are authorized in the context of a replenishment of calcium and vitamin D. For the registration process, participants are almost always supplemented with calcium and vitamin D, both in the placebo group as in the group with active drug (Table 1).

The current trend is to analyze the intake of calcium in the diet through dietary surveys. If it is insufficient, supplement if possible through the diet or, otherwise, prescribed supplements[17]. Regarding vitamin D, determining the plasma levels of 25-OH-vitamin D is recommended. If they are below 20 ng/ml, supplement with a dose of 800-1,000 IU/day. Different clinical practice guides, both national[18] and international[19] advocate this practice.

In addition, insufficient levels of vitamin D have been described associated with an inadequate response of osteoporosis drugs. In a study that included 210 women with postmenopausal osteoporosis treated with bisphosphonates (mostly oral; only 38 patients with zoledronate) it was observed that those patients who maintained levels of 25-OH-vitamin D ≥33 ng/ml presented a probability 4, 5 times greater than presenting a favorable response to antiresorptive treatment[20]. Along the same lines, an observational study, carried out with the patients of the SIDIAP database (System of Information for the Development of Research in Primary Care) that initiated an oral bisphosphonate between 2006-2007, observed that the probability of response Inadequate to treatment, assessed as the presence of any fracture during treatment, was 2.7 times more likely in those patients with vitamin D insufficiency[21] .

In an analysis of the FOCUS-D clinical trial (Fosavance vs. standard care-use and study of vitamin D) of patients treated with alendronate and vitamin D it was found that plasma levels of vitamin D correlated with changes in BMD, both at lumbar level as well as femoral, in patients treated with alendronate[22].

In a study conducted on 153 women with postmenopausal osteoporosis who were to receive a first dose of zoledronate, it was observed that 25-OH-vitamin D levels were lower in those who had an acute phase reaction, so that those with 25-OH-vitamin D levels <30 ng/ml presented 4.2 times the risk of pre-

Table 1. Use of calcium and vitamin D in an adjunctive way in the treatment of osteoporosis with drugs currently approved by the EMA* and/or the FDA*

Drug	Study (Author)	Supplement calcium	Supplement vitamin D	Percentage supplemented
Alendronate	FIT (Black et al.)[28]	500 mg	250 IU	82%
Risedronate	VERT (Harris et al.)[29]	500 mg	500 IU	100%
Ibandronate	BONE (Delmas et al.)[30]	500 mg	400 IU	100%
Zoledronate	HORIZON (Black et al.)[31]	1,000 mg	400 – 1,000 IU	100%
Raloxifene	MORE (Ettinger et al.)[32]	500 mg	400 – 600 IU	100%
Bazedoxifene	(Silverman et al.)[33]	<1,200 mg	400 – 800 IU	100%
Teriparatide	Fracture Prevention Trial (Neer et al.)[34]	1,000 mg	400 – 1,200 IU	100%
Denosumab	FREEDOM (Cummings et al.)[35]	>1,000 mg	400 – 800 IU	100%
Romosozumab	FRAME (Cosman et al.)[36]	500 –1,000 mg	600 – 800 IU	100%

* EMA: European Medicines Agency; FDA: Food and Drugs Administration.

senting said reaction[23]. In patients treated with zoledronate, the assessment of plasma levels of creatinine, calcemia and 25-OH-vitamin D is recommended, being necessary to correct them before administration to avoid the occurrence of clinically significant hypocalcemia.

A population-based Taiwanese observational study analyzed the relationship between the use of bisphosphonates and the occurrence of atrial fibrillation, observing an increased risk in patients treated with bisphosphonates, but a potential beneficial effect of vitamin D reducing the occurrence of atrial fibrillation[24].

Regarding denosumab, a study conducted of 41 patients with primary osteoporosis, where 18 received only denosumab and 23 denosumab together with 1,200 mg calcium and 400 IU of vitamin D per day, observed a greater change in BMD in the combined group compared with the group treated exclusively with denosumab[25]. At 12 months, an increase of 6% was observed at lumbar level in the monotherapy group and 8.9% in the combined treatment group, a non-significant difference (p=0.22). At femoral level, an increase of 1.2% and 3.6% was observed at 12 months respectively, a statistically significant difference (p<0.05). Although no patient presented hypocalcemia, the addition of calcium and vitamin D, was not associated with a decrease in calcemia levels, a fact that was observed in the monotherapy group. The authors conclude the need to supplement patients treated with denosumab with calcium and vitamin D.

The VERO clinical trial (The vertebral fracture treatment comparisons in osteoporotic women) has recently been published, where 1,360 women with established postmenopausal osteoporosis were randomized to receive teriparatide or risedronate for two years, together with 500-1,000 mg/day of calcium and 400- 800 IU/day of vitamin D (mainly cholecalciferol). A post-hoc analysis[26] observed that patients treated with teriparatide presented at six months a decrease in the average levels of 25-OH-vitamin D (from 31.9 ng/ml to 24.5 ng/ml), a fact that did not It was observed in patients treated with risedronate (from 31.5 ng/ml to 32.2 ng/ml). The percentage of patients with insufficient levels of vitamin D increased in the teriparatide group, while the risedronate group decreased. There were, however, no significant differences in the anti-fracture effect in relation to 25-OH-vitamin D levels.

Finally, commenting that a cost-effectiveness study concluded that the use of calcium and vitamin D supplements in women and men >60 years with osteoporosis was cost-effective, recommending its use from an economic perspective, even in patients treated with other osteoporosis drugs[27].

Conclusion

Correcting the levels of calcium and vitamin D is recommended, preferably through diet or the use of supplements, in patients with osteoporosis who are going to receive an antiresorptive or osteoforming drug. It is a cost-effective intervention. In addition, the correction of vitamin D levels can be associated with a decrease in the risk of falls, and therefore with a lower risk of osteoporotic fracture.

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Bibliography

1. Seeman E. Structural basis of growth-related gain and age-related loss of bone strength. Rheumatology (Oxford). 2008;47(Suppl 4):iv2-8.
2. Hernlund E, Svedbom A, Ivergård M, Compston J, Cooper C, Stenmark J, et al. Osteoporosis in the European Union: medical management, epidemiology and economic burden. A report prepared in collaboration with the International Osteoporosis Foundation (IOF) and the European Federation of Pharmaceutical Industry Associations (EFPIA). Arch Osteoporos. 2013;8:136.
3. Cummings SR, Kelsey JL, Nevitt MC, O'Dowd KJ. Epidemiology of osteoporosis and osteoporotic fractures. Epidemiol Rev. 1985;7:178-208.
4. Mendoza N, De Teresa C, Cano A, Godoy D, Hita-Contreras F, Lapotka M, et al. Benefits of physical exercise in postmenopausal women. Maturitas. 2016;93:83-8.
5. Rizzoli R. Nutritional aspects of bone health. Best Pract Res Clin Endocrinol Metab. 2014;28:795-808.
6. Gehlert S, Bloch W, Suhr F. Ca2+-dependent regulations and signaling in skeletal muscle: from electro-mechanical coupling to adaptation. Int J Mol Sci. 2015;16:1066-95.
7. Rizzoli R, Stevenson JC, Bauer JM, van Loon LJC, Walrand S, Kanis JA, et al. The role of dietary protein and vitamin D in maintaining musculoskeletal health in postmenopausal women: a consensus statement from the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO). Maturitas. 2014;79:122-32.
8. Beaudart C, Buckinx F, Rabenda V, Gillain S, Cavalier E, Slomian J, et al. The effects of vitamin D on skeletal muscle strength, muscle mass, and muscle power: a systematic review and meta-analysis of randomized controlled trials. J. Clin. Endocrinol Metab. 2014; 99:4336-45.
9. Bischoff-Ferrari HA, Dawson-Hughes B, Staehelin HB, Orav JE, Stuck AE, Theiler R, et al. Fall prevention with supplemental and active forms of vitamin D: a meta-analysis of randomised controlled trials. BMJ. 2009;339:b3692.
10. LeBlanc ES, Chou R. Vitamin D and Falls-Fitting new data with current guidelines. JAMA Intern Med. 2015; 175:712-3.
11. Kalyani RR, Stein B, Valiyil R, Manno R, Maynard JW, Crews DC. Vitamin D treatment for the prevention of falls in older adults: systematic review and meta-analysis. J Am Geriatr Soc. 2010; 58:1299-310.
12. Harvey NC, Biver E, Kaufman J-M, Bauer J, Branco J, Brandi ML, et al. The role of calcium supplementation in healthy musculoskeletal ageing. Osteoporos Int. 2017;28:447-62.
13. Institute of Medicine (US) Committee to Review Dietary Reference Intakes for Vitamin D and Calcium. Dietary Reference Intakes for Calcium and Vitamin D. Washington, D.C.: National Academies Press; 2011.
14. Tai V, Leung W, Grey A, Reid IR, Bolland MJ. Calcium intake and bone mineral density: systematic review and meta-analysis. BMJ. 2015;351:h4183.
15. Reid IR, Bolland MJ. Skeletal and nonskeletal effects of vitamin D: is vitamin D a tonic for bone and other tissues? Osteoporos Int. 2014;25:2347-57.
16. Clifton-Bligh PB, Nery ML, Clifton-Bligh RJ, Fulcher GR, Baber R. Changes in bone mineral density related to changes in serum 25-OH vitamin D concentrations over a two-year period in postmenopausal women. Endocrine. 2017;58:587-90.
17. Cano A, Chedraui P, Goulis DG, Lopes P, Mishra G, Mueck A, et al. Calcium in the prevention of postmenopausal osteoporosis: EMAS clinical guide. Maturitas. 2018;107:7-12.
18. González-Macías J, del Pino-Montes J, Olmos JM, Nogués X. Clinical practice guidelines for postmenopausal, glucocorticoid-induced and male osteoporosis. Spanish Society for Research on Bone and Mineral Metabolism (3rd updated version 2014). Rev Clin Esp. 2015;215:515-26.
19. Kanis JA, Cooper C, Rizzoli R, Reginster J-Y. European guidance for the diagnosis and management of osteoporosis in postmenopausal women. Osteoporos Int. 2019;30:3-44.
20. Carmel AS, Shieh A, Bang H, Bockman RS. The 25(OH)D level needed to maintain a favorable bisphosphonate response is ≥33 ng/ml. Osteoporos Int. 2012;23:2479-87.
21. Prieto-Alhambra D, Pagès-Castellà A, Wallace G, Javaid MK, Judge A, Nogués X, et al. Predictors of fracture while on treatment with oral bisphosphonates: a population-based cohort study. J Bone Miner Res. 2014;29:268-74.
22 Roux C, Binkley N, Boonen S, Kiel DP, Ralston SH, Regnister J-Y, et al. Vitamin D status and bone mineral density changes during alendronate treatment in postmenopausal osteoporosis. Calcif Tissue Int. 2014;94:153-7.
23. Crotti C, Watts NB, De Santis M, Ceribelli A, Fabbriciani G, Cavaciocchi F, et al. Acute phase reactions after zoledronic acid infusion: protective role of 25-hydroxyvitamin D and previous oral bisphosphonate therapy. Endocr Pract. 2018;24:405-10.
24. Yang HY, Huang JH, Chiu HW, Lin YK, Hsu CY, Chen YJ. Vitamin D and bisphosphonates therapies for osteoporosis are associated with different risks of atrial fibrillation in women: A nationwide population-based analysis. Medicine (Baltimore). 2018;97:e12947.
25. Nakamura Y, Suzuki T, Kamimura M, Murakami K, Ikegami S, Uchiyama S, et al. Vitamin D and calcium are required at the time of denosumab administration during osteoporosis treatment. Bone Res. 2017;5:17021.
26. Minisola S, Marin F, Kendler DL, Geusens P, Zerbini CAF, Russo LA, et al. Serum 25-hydroxy-vitamin D and the risk of fractures in the teriparatide versus risedronate VERO clinical trial. Arch Osteoporos. 2019;14:10.
27. Hiligsmann M, Ben Sedrine W, Bruyere O, Evers SM, Rabenda V, Reginster J-Y. Cost-effectiveness of vitamin D and calcium supplementation in the treatment of elderly women and men with osteoporosis. Eur J Public Health. 2015; 25:20-5.
28. Black DM, Thompson DE, Bauer DC, Ensrud K, Musliner T, Hochberg MC, et al. Fracture risk reduction with alendronate in women with osteoporosis: the Fracture Intervention Trial. J Clin Endocrinol Metab. 2000;85:4118-24.
29. Harris ST, Watts NB, Genant HK, McKeever CD, Hangartner T, Keller M, et al. Effects of risedronate treatment on vertebral and nonvertebral fractures in women with postmenopausal osteoporosis: a randomized controlled trial. Vertebral Efficacy With Risedronate Therapy (VERT) Study Group. JAMA. 1999;282:1344-52.
30. Delmas PD, Recker RR, Chesnut CH, Skag A, Stakkestad JA, Emkey R, et al. Daily and intermittent oral ibandronate normalize bone turnover and provide significant reduction in vertebral fracture risk: results from the BONE study. Osteoporos Int. 2004; 15:792-8.
31. Black DM, Delmas PD, Eastell R, Reid IR, Boonen S, Cauley JA, et al. Once-yearly zoledronic acid for treatment of postmenopausal osteoporosis. N Engl J Med. 2007;356:1809–22.
32. Ettinger B, Black DM, Mitlak BH, Knickerbocker RK, Nickelsen T, Genant HK, et al. Reduction of vertebral fracture risk in postmenopausal women with osteoporosis treated with raloxifene: results from a 3-year randomized clinical trial. Multiple Outcomes of Raloxifene Evaluation (MORE) Investigators. JAMA. 1999; 282:637-45.
33. Silverman SL, Christiansen C, Genant HK, Vukicevic S, Zanchetta JR, de Villiers TJ, et al. Efficacy of bazedoxifene in reducing new vertebral fracture risk in postmenopausal women with osteoporosis: results from a 3-year, randomized, placebo-, and active-controlled clinical trial. J Bone Miner Res. 2008;23:1923-34.
34. Neer RM, Arnaud CD, Zanchetta JR, Prince R, Gaich GA, Reginster JY, et al. Effect of parathyroid hormone (1-34) on fractures and bone mineral density in postmenopausal women with osteoporosis. N Engl J Med. 2001;344:1434-41.
35. Cummings SR, San Martin J, McClung MR, Siris ES, Eastell R, Reid IR, et al. Denosumab for prevention of fractures in postmenopausal women with osteoporosis. N Engl J Med. 2009;361:756-65.
36. Cosman F, Crittenden DB, Adachi JD, Binkley N, Czerwinski E, Ferrari S, et al. Romosozumab treatment in postmenopausal women with osteoporosis. N Engl J Med. 2016;375:1532-43.

Self assessment test

1. Regarding the effect of supplementation on muscle with vitamin D alone compared with calcium and vitamin D, indicate the answer:

a. Improves muscle strength
b. It improves muscle mass
c. It improves muscle power
d. Increase the number of myocytes

2. Of the reference studies involving the different drugs, a greater amount of vitamin D was attained with the drug and (acronym):

a. Alendronate (FIT)
b. Risedronate (VERT)
c. Raloxifene (MORE)
d. None of the above

3. In the reference study with zoledronate, we can affirm that it is true:

a. Both the treated and placebo groups received calcium and vitamin D
b. The reaction that occurs in the acute phase seems to be more intense when patients presented low levels of vitamin D
c. There is some risk of hypocalcemia with the administration of zoledronate
d. All of the above is true

4. In the treatment of osteoporosis calcium and vitamin D administration is advised, since:

a. In all reference studies, calcium and vitamin D have been administered in both groups receiving the drug as a placebo
b. This administration is cost-effective
c. It is advisable to use pharmacological supplementation only when it has not been possible to do so through diet
d. All of the above are true

5. Regarding the physiology of calcium and vitamin D, indicate the correct answer:

a. Calcium deficit can condition the obtaining of a lower peak bone mass
b. Vitamin D deficiency can cause osteomalacia in adults
c. Vitamin D deficiency can cause rickets in children
d. All of the above is true

Correct answers can be found on pages 23 and 24

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Role of calcium and vitamin D in treating hip fracture patients

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Introduction

The proximal femur fracture, or hip fracture, is the most serious complication of osteoporosis, due to its high mortality and morbidity, as well as the significant social, economic and welfare cost it entails. In fact, the hip fracture is capable, on its own, of decreasing life expectancy in almost two years and one in five patients who suffer from it will require permanent health care[1]. Risk factors that favor this type of fracture include a greater tendency to fall and a decrease in bone resistance.

Since the discovery of vitamin D in 1922, it has been associated not only with bone health but also with muscle health[2]. Therefore, and although there is no evidence that determines its effectiveness, calcium and vitamin D administration is recommended for every patient with osteoporosis, to avoid their deficiency, which may be harmful. Thus, in most clinical practice guidelines, treatment with antiresorptive or anabolic drugs must be accompanied by an adequate intake of vitamin D, in addition to an appropriate amount of calcium, which usually ranges between 1,000 and 1,200 mg daily[3-5].

Serum vitamin D levels in patients with osteoporosis

Calcium should be administered with the diet, whenever possible, while vitamin D is recommended to be taken as supplements. One controversial aspect is that of the serum levels of 25(OH) vitamin D [25(OH)D] that osteoporosis patients should reach, although most authors and scientific societies, including Spanish ones, consider that they would recommend serum concentrations to be above 30 ng/ml[6-9]. To achieve these aims, a daily dose of 800 to 1,000 IU of vitamin D (in Europe the vitamin D used is vitamin D3, known as colecalciferol) is advised, although its weekly, biweekly or monthly equivalent can also be administered[10]. This recommendation is especially relevant in patients who have already suffered a hip fracture. It is well known that the history of fragility fracture is, together with age, sex and bone mineral density (BMD), one of the main risk factors for osteoporotic fractures[3-5]. In fact, in the fracture risk prediction scales, such as the FRAX® scale or the Q-Fracture® scale, the presence of a fracture implies an increased risk of fracture in subsequent years. On the other hand, the risk of fracture is especially important if the fracture is recent. Thus, in a study carried out in Iceland[11], people with a history of major osteoporotic fracture (hip, radius, humerus or clinical vertebral) reportedly presented an especially high risk of suffering another fracture in the first 24 months and that subsequently it stabilized, although always remaining above the risk of the population without a history of fracture. In the specific case of hip fracture, refracture incidence can reach up to 10% during the first years[12].

On the other hand, the prevalence of hypovitaminosis D (serum levels of 25OHD <20 ng/ml) is very high in patients suffering from a hip fracture, reaching, for example, 36% in Finland[13], 40-68% in United Kingdom[14], between 50-78% in the US[15], between 62-90% in Japan[16] and between 67-91% in Spain[17]. These rates are much higher than those found in people without hip fracture, although lower than those found in institutionalized subjects[18].

However, only a small percentage of patients who suffer a hip fracture receive antiosteoporotic treatment, including calcium and vitamin D supplements. Thus, in a study that included more than 85,000 hip fracture patients from different geographical areas (the USA, Spain and Korea), it was observed that only 11% of American patients, 25% of Spaniards, and 39% of Koreans, followed some type of antiosteoporotic treatment three months after be discharged after the fracture[19].

In a similar study[20] carried out in the USA involving almost 100,000 patients with hip fractures, less than 30% received treatment during the first 12 months after discharge and this percentage decreased in recent years (2002-2011 period). Finally, a recent work carried out in Spain[21] indicates that only 21% of hip fracture patients receive antiosteoporotic treatment

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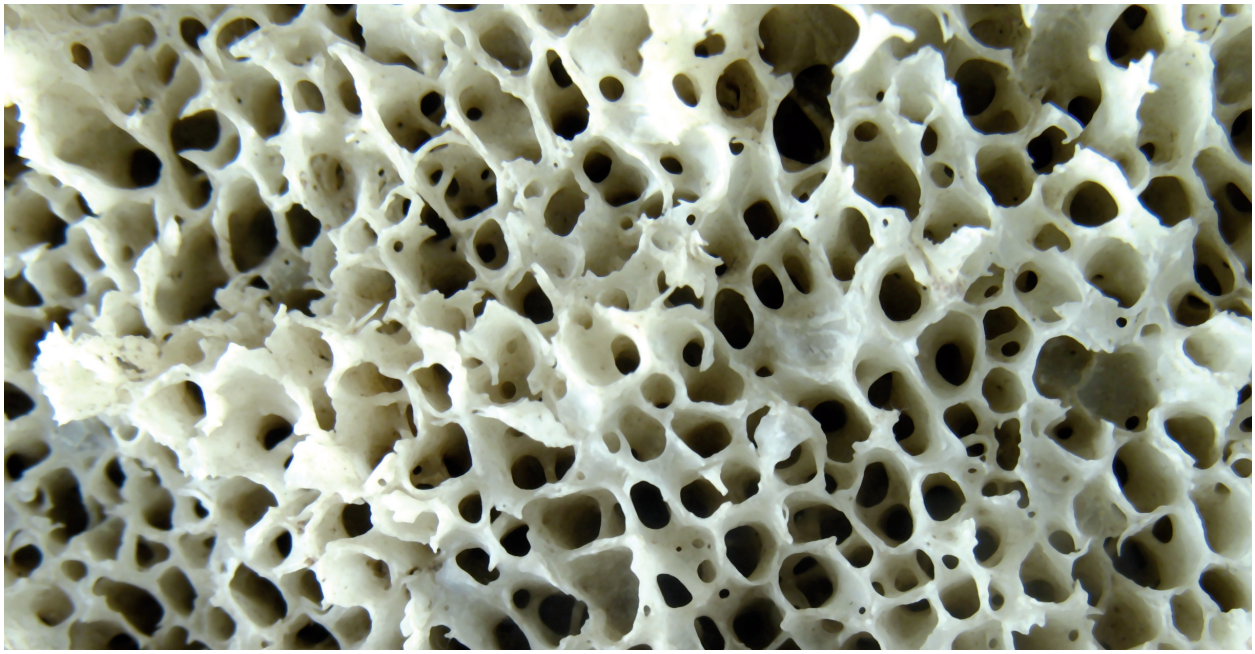

after hospital discharge, increasing this percentage to 32% and 38%, one month and 4 months afterwards, respectively. Nor is the percentage of patients receiving only calcium and/or vitamin D much higher. Thus, in a study conducted in Finland with more than 30,000 patients who had suffered a hip fracture, 13% of men and 22% of women received treatment with calcium and/or vitamin D, while this percentage reached 8% and 27%, respectively, in the case of bisphosphonates or other antiosteoporotic drugs[22]. In another study in North America, Europe and Australia, more than half of the patients who underwent surgery after suffering a hip fracture, reportedly did not take calcium and/or vitamin D supplements, or did so irregularly, two months after being discharged[23]. This percentage was close to 50% in another study carried out in Italy[24].

Hypovitaminosis D in patients with hip fracture

In the absence of preventive treatment, hypovitaminosis D in patients who have suffered a hip fracture can cause proximal muscle weakness and reduce dynamic balance and gait speed[7], which would make it difficult to mobilize patients during the postoperative and rehabilitation period. In this regard, Di Monaco et al.[25] observed that patients with hip fractures who had levels of 25(OH)D below 12 ng/ml had a worse recovery than those who had levels between 12 and 20 ng/ml, and these, in turn, were associated with a worse recovery than those with value between 21 and 29 ng/ml. On the contrary, no significant differences were found between this last group and those patients with levels ≥30 ng/ml. In addition, in some randomized controlled trials, although with a small number of patients, benefits have been reported in subjects who received vitamin D supplements after suffering a hip fracture. Thus, Harwood et al.[26] observed that oral or parenteral vitamin D reduced the risk of falls after one year of presenting a hip fracture, in a study with 150 women who remained functionally independent before the fracture. Mak et al.[27] found that a single dose of cholecalciferol load (250,000 IU) followed by 800 IU daily, reduced the risk of falls compared to the isolated daily dose in 218 patients (77% women) followed for 26 weeks. Finally, Bishoff-Ferrari et al.[12] observed that the administration of high doses of vitamin D (2,000 IU/day) to patients discharged after suffering a hip fracture, reduced the rate of readmissions during the first 40% year. These authors[28] have also observed that performing physical exercise at home together with the administration of 800 IU of vitamin D3 improved functional recovery after a hip fracture.

As stated above, calcium and vitamin D play an essential role in the treatment of osteoporosis. First, this is because, although there is no conclusive evidence of its effectiveness in reducing fractures when used in isolation, in virtually all clinical trials conducted to demonstrate the anti-fractural effects of antiosteoporotic medication, Patients received oral calcium and vitamin D supplements[3-5]. Secondly, the existence of hypovitaminosis D increases the risk of fragility fractures and reduces the protection against fractures provided by some drugs widely used in clinical practice in the treatment of patients with osteoporosis[24,29,30]. In the specific case of the hip fracture, Degli Esposti et al.[24] carried out a cohort study that included 3,475 patients 50 years of age or older hospitalized for a vertebral or hip fracture during the years 2011 to 2015, and they were followed for 3 years. These authors found that the risk of refracture was 44% lower in patients treated with anti-osteoporotic drugs (anti-resorptive or anabolic) along with calcium and/or vitamin D, compared to those who did not receive supplements.

In addition, the incidence of new fractures was almost 65% lower in patients who received calcium/vitamin D supplements compared to those who only received antiresorptive or anabolic therapy[24].

On the other hand, mild and, especially, severe hypovitaminosis may increase the symptomatic hypocalcaemia that is sometimes observed after the administration of potent parenteral antiresorptive drugs, such as zoledronic acid or denosumab, widely used in the treatment of patients with hip fracture. In fact, in the classic study by Lyles et al.[31] in which a 28% reduction in mortality was demonstrated in hip fracture patients treated with zoledronic acid, all patients also received calcium and vitamin supplements. D. In this regard, it is worth commenting that the beneficial effect on mortality has also been observed with other antiosteoporotic drugs, including calcium and vitamin D supplements themselves[32]. For example, in the aforementioned cohort of Degli Esposti et al.[24], patients treated with antiresorptive or anabolic drugs, in addition to calcium and vitamin D, presented a 64% reduction in the risk of overall mortality in relation to those who did not They received treatment. In addition, mortality rates were even lower among treated patients receiving calcium and/or vitamin D supplements. Finally, Cancio et al.[33], in a recent retrospective study conducted in our country, with more than 30,000 patients out of 65 or more years with hip fracture followed for two years, observed that treatment with calcium and/or vitamin D reduced total mortality by 16% (HR: 0.84; 95% CI 0.79-0.88; p<0.001).

Conclusion

Although there is no evidence of its effectiveness when administered in isolation, it is considered that calcium and vitamin D should be prescribed to every patient with osteoporosis, especially if they have suffered a fragility fracture. In our usual clinical practice, it is advisable that patients with hip fractures receive an adequate intake of vitamin D (daily dose between 800-1,000 IU), in addition to an appropriate amount of calcium (between 1,000-1,200 mg/day), preferably with diet.

Conflict of interests: The authors declare no conflict of interest.

Bibliography

1. Norton R, Butler M, Robinson E, Lee-Joe T, Campbell AJ. Declines in physical functioning attributable to hip fracture among older people: a follow-up study of case-control participants. Disabil Rehabil. 2000;22:345-51.
2. Quesada-Gómez JM, Sosa Henríquez M. Vitamina D y función muscular. Rev Osteoporos Metab Miner. 2019;11:3-5.
3. Cosman F, de Beur SJ, LeBoff MS, Lewiecki EM, Tanner B, Randall S, et al. Clinician's Guide to Prevention and Treatment of Osteoporosis. Osteoporos Int. 2014;25:2359-81.
4. González-Macías J, Del Pino-Montes J, Olmos JM, Nogués X; en nombre de la Comisión de Redacción de las Guías de Osteoporosis de la SEIOMM. Guías de práctica clínica en la osteoporosis postmenopáusica, glucocorticoidea y del varón. Sociedad Española de Investigación Ósea y del Metabolismo Mineral (3ª. Versión actualizada 2014). Rev Clin Esp. 2015;215:515-26.
5. Compston J, Cooper A, Cooper C, Gittoes N, Gregson C, Harvey N, et al; National Osteoporosis Guideline Group (NOGG). UK clinical guideline for the prevention and treatment of osteoporosis. Arch Osteoporos. 2017;12:43.
6. Dawson-Hughes B, Mithal A, Bonjour JP, Boonen S, Burckhardt P, Fuleihan GE, et al. IOF position statement vitamin D recommendations for older adults. Osteoporos Int. 2010;21:1151-4.
7. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2011;96:1911-30.
8. Varsavsky M, Rozas Moreno P, Becerra Fernández A, Luque Fernández I, Quesada Gómez JM, Ávila-Rubio V, et al.; en representación del Grupo de Trabajo de Osteoporosis y Metabolismo Mineral de la Sociedad Española de Endocrinología y Nutrición. Recomendaciones de vitamina D para la población general. Endocrinol Diabetes Nutr. 2017;64 (Suppl 1):7-14.
9. Gómez de Tejada Romero MJ, Sosa Henríquez M, Del Pino Montes J, Jódar Gimeno E, Quesada Gómez JM, Cancelo Hidalgo MJ, et al. Documento de posición sobre las necesidades y niveles óptimos de Vitamina D. Sociedad Española de Investigación Ósea y Metabolismo Mineral (SEIOMM) y Sociedades afines. Rev Osteoporosis Metab Miner. 2011;3:53-64.
10. Olmos JM, Arnaiz F, Hernández JL, Olmos-Martínez JM, González Macías J. Calcifediol mensual frente a calcifediol quincenal en el tratamiento de pacientes osteoporóticos. Estudio en la vida real. Rev Osteoporos Metab Miner. 2018;10:89-95.
11. Johansson H, Siggeirsdóttir K, Harvey NC, Odén A, Gudnason V, McCloskey E, et al. Imminent risk of fracture after fracture. Osteoporos Int. 2017;28:775-80.
12. Bischoff-Ferrari HA, Dawson-Hughes B, Platz A, Orav EJ, Stähelin HB, Willett WC, et al. Effect of high-dosage cholecalciferol and extended physiotherapy on complications after hip fracture: a randomized controlled trial. Arch Intern Med. 2010;170:813-20.
13. von Knorring J, Slätis P, Weber TH, Helenius T. Serum levels of 25-hydroxyvitamin D, 24,25-dihydroxyvitamin D and parathyroid hormone in patients with femoral neck fracture in southern Finland. Clin Endocrinol. (Oxf) 1982;17:189-94.
14. Dixon T, Mitchell P, Beringer T, Gallacher S, Moniz C, Patel S, et al. An overview of the prevalence of 25hydroxy-vitamin D inadequacy amongst elderly patients with or without fragility fracture in the United Kingdom. Curr Med Res Opin. 2006;22:405-15.
15. LeBoff MS, Kohlmeier L, Hurwitz S, Franklin J, Wright J, Glowacki J. Occult vitamin D deficiency in postmenopausal US women with acute hip fracture. JAMA. 1999;281:1505-11.
16. Nakano T, Tsugawa N, Kuwabara A, Kamao M, Tanaka K, Okano T. High prevalence of hypovitaminosis D and K in patients with hip fracture. Asia Pac J Clin Nutr. 2011;20:56-61.
17. Larrosa M, Gomez A, Casado E, Moreno M, Vázquez I, Orellana C, et al. Hypovitaminosis D as a risk factor of hip fracture severity. Osteoporos Int. 2012;23:607-14.
18. Mesa Ramos M. Vitamina D y fracturas por fragilidad. Rev Osteoporos Metab Miner. 2017;9(Supl 1):S40-4.
19. Kim SC, Kim MS, Sanfélix-Gimeno G, Song HJ, Liu J, Hurtado I, et al. Use of osteoporosis medications after hospitalization for hip fracture: a cross-national study. Am J Med. 2015;128:519-26.
20. Solomon DH, Johnston SS, Boytsov NN, McMorrow D, Lane JM, Krohn KD. Osteoporosis medication use after hip fracture in U.S. patients between 2002 and 2011. J Bone Miner Res. 2014;29:1929-37.
21. Prieto-Alhambra D, Reyes C, Sainz MS, González-Macías J, Delgado LG, Bouzón CA, et al. In-hospital care, complications, and 4-month mortality following a hip or proximal femur fracture: the Spanish registry of osteoporotic femur fractures prospective cohort study. Arch Osteoporos. 2018;13:96.
22. Nurmi-Lüthje I, Sund R, Juntunen M, Lüthje P. Post-hip fracture use of prescribed calcium plus vitamin D or vitamin D supplements and antiosteoporotic drugs is associated with lower mortality: a nationwide study in Finland. J Bone Miner Res. 2011;26:1845-53.
23. Sprague S, Madden K, Slobogean G, Petrisor B, Adachi JDR, Bogoch E, et al. A missed opportunity in bone health: vitamin D and calcium use in elderly femoral neck fracture patients following arthroplasty. Geriatr Orthop Surg Rehabil. 2017;8:215-24.
24. Degli Esposti L, Girardi A, Saragoni S, Sella S, Andretta M, Rossini M, et al; on the behalf of the Study group. Use of antiosteoporotic drugs and calcium/vitamin D in patients with fragility fractures: impact on re-fracture and mortality risk. Endocrine. 2018 Dec 4. doi: 10.1007/s12020-018-1824-9. [Epub ahead of print].
25. Di Monaco M, Castiglioni C, Di Carlo S, La Marmora E, Filipovic I, Milano E, et al. Classes of vitamin D status and functional outcome after hip fracture: a prospective, short-term study of 1350 inpatients. Eur J Phys Rehabil Med. 2019;55:56-62.
26. Harwood RH, Sahota O, Gaynor K, Masud T, Hosking DJ; Nottingham Neck of Femur (NONOF) Study. A randomised, controlled comparison of different calcium and vitamin D supplementation regimens in elderly women after hip fracture: The Nottingham Neck of Femur (NONOF) Study. Age Ageing. 2004;33:45-51
27. Mak JCS, Klein L, Mason RS, Cameron ID. Contemporary pain management in elderly patients after hip fracture surgery: cross-sectional analyses at baseline of a randomized controlled trial. Clin J Pain. 2015;31:788-93.
28. Stemmle J, Marzel A, Chocano-Bedoya PO, Orav EJ, Dawson-Hughes B, Freystaetter G, et al. Effect of 800 IU versus 2000 IU vitamin D3 with or without a simple home exercise program on functional recovery after hip fracture: a randomized controlled trial. J Am Med Dir Assoc. 2019 May;20(5):530-6.
29. Adami S, Giannini S, Bianchi G, Sinigaglia L, Di Munno O, Fiore CE, et al. Vitamin D status and response to treatment in postmenopausal osteoporosis. Osteoporos Int. 2009;20:239-44.
30. Díez-Pérez A, Olmos JM, Nogués X, Sosa M, Díaz-Curiel M, Pérez-Castrillón JL, et al. Risk factors for prediction of inadequate response to antiresorptives. J Bone Miner Res. 2012;27:817-24.
31. Lyles KW, Colón-Emeric CS, Magaziner JS, Adachi JD, Pieper CF, Mautalen C, et al. HORIZON recurrent fracture trial. Zoledronic acid and clinical fractures and mortality after hip fracture. N Engl J Med. 2007;357:1799-1809.
32. Bolland MJ, Grey AB, Gamble GD, Reid IR. Effect of osteoporosis treatment on mortality: a meta-analysis. J Clin Endocrinol Metab. 2010; 95:1174-81.
33. Cancio JM, Vela E, Santaeugènia S, Clèries M, Inzitari M, Ruiz D. Influence of demographic and clinical characteristics of elderly patients with a hip fracture on mortality: A retrospective, total cohort study in North-East Spain. Bone. 2018;117:123-9.

Self assessment test

1. The most serious osteoporotic fracture is:

a. *Vertebral*
b. *Distal radius*
c. *Humerus*
d. *None of the above*

2. The prevalence of vitamin D deficiency, defined as (serum 25OHD levels <20 ng/ml) is very high in patients suffering from a hip fracture, reaching in Spain figures between:

a. *36-40%*
b. *40-68%*
c. *50-78%*
d. *67-91%*

3. The presence of a fracture implies an increased risk of fracture in subsequent years. In the specific case of the hip fracture, the incidence of refracture can reach:

a. *5%*
b. *10%*
c. *15%*
d. *20%*

4. In randomized studies it has been proven that the administration of vitamin D produces:

a. *Fall risk reduction*
b. *Reduction of the risk of new hip fractures*
c. *Reduction of the risk of readmissions after a hip fracture*
d. *All of the above is true*

5. Point out the answer that seems false:

a. *Calcium and vitamin D should be prescribed to every patient with osteoporosis*
b. *The amount of vitamin D should range between 800 and 1,000 IU/day*
c. *The amount of calcium should range between 1,000 and 1,200 mg/day*
d. *Pharmacological supplementation is preferable*

Correct answers can be found on pages 23 and 24

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Self assessment test: correct answers

Myths, stories and legends about calcium and vitamin D

Sosa Henríquez M, Gómez de Tejada Romero MJ

1. The mandatory calcium losses are:
d. Urine and feces about 1,000 mg daily
Compulsory calcium losses are estimated at about 1,000 mg daily, of which around 200 mg is due to calciuria and the remaining 800 mg due to fecal losses, due to calcium contained in pancreatic juices and calcium ingested and not absorbed.

2. A woman after menopause is advised to ingest daily:
d. 1,500 mg of calcium
In menopause, daily calcium recommendations have been estimated at 1,500 mg daily by the National Health Institute (NIH).

3. The Spanish paradox of vitamin D comes to say:
d. All of the above is false
The Spanish vitamin D paradox refers to the fact that vitamin D levels, measured by its reserve metabolite, calcidiol. They are higher in the Nordic countries than in Spain, which is because, in these countries, given the few hours of sunshine in the autumn and winter months, their food is fortified with vitamin D, while in Spain, by cultural reasons, we take little advantage of the hours of sun we have.

4. Which of the following foods has a higher calcium content in milligrams per 100 g of edible portion:
d. Cured Manchego cheese
100 g of cured Manchego cheese provide 1,200 mg of calcium, while none of the other options included in the question reach 200 mg.

5. What is the prevalence of hypovitaminosis D in medical students of the University of Las Palmas de Gran Canaria? (25HCC values below 30 ng/mL):
d. 61%
Medical students at the University of Las Palmas de Gran Canaria should theoretically have optimal levels of vitamin D, since they have sun all year round, are young and generally healthy and have knowledge of the physiology of vitamin D. Although there is sunshine available to them, however, they do not take advantage of it, for lifestyle reasons.

Recommendations of scientific societies on the calcium and vitamin D supplementation in osteoporosis

Gómez de Tejada Romero MJ, Sosa Henríquez M

1. For the National Osteoporosis Society (NOS) of the United Kingdom, vitamin D deficiency occurs when serum levels of 25 hydroxyvitamin D25 (OH)D are lower than:
d. 10 ng/mL
In these guidelines, the British, establish as vitamin D deficiency serum levels of 25(OH)D below 10 ng/ml (30 nmol/l), and, recognizing that there is no consensus on this, they do support the majority in favor of considering as inappropriate values those that are between 20 and 30 ng/ml (at least in some populations).

2. For the American Association of Clinical Endocrinologists/American College of Endocrinology, patients over 50 must maintain a daily calcium intake of at least:
d. 1,500 mg
For the American Association of Clinical Endocrinologists/American College of Endocrinology, patients should be advised to maintain an adequate calcium intake of 1,200 mg/day for women over 50, which if not achieved by diet should be supplemented with supplements.

3. For the Spanish Society of Bone Research and Mineral Metabolism (SEIOMM), patients with osteoporosis should receive a daily intake of calcium and vitamin D from:
d. None of the above
For the Spanish Society of Bone Research and Mineral Metabolism (SEIOMM), patients with osteoporosis should receive a contribution of 1,000-1,200 mg/day of calcium and 800 IU/day of vitamin D, so that, if these figures are not achieved with the diet, supplements must be added.

4. For the Endocrine Society, adults over 50 years of age must reach serum values of 25(OH)D higher than:
a. 30 ng/mL
The Endocrine Society recommends that those over 50 years of age raise blood levels of 25(OH)D above 30 ng/ml. At least 1,500-2,000 IU of vitamin D supplement may be required. In this regard, they also recommend use vitamin D2 or D3.

5. One of the following recommendations of the (SEEN) on vitamin D is false:
d. Systematic supplementation is recommended in all adults under 50 years of age to obtain improvement in bone health
There are no data supporting this recommendation.

Rev Osteoporos Metab Miner. 2019;11(Supl 1):S23-24

Self assessment test: correct answers

The role of calcium and vitamin D in the prevention and treatment of osteoporosis

Martínez-Laguna D

1. Regarding the effect of supplementation on muscle with vitamin D alone compared to calcium and vitamin D, indicate the answer:
a. Improves muscle strength
A systematic review suggests a low but significant positive effect of supplementation on muscle strength, but not on muscle mass or power. No differences were observed between the use of vitamin D supplements compared to vitamin D supplements with calcium.

2. Of the reference studies with the different drugs, in which a greater amount of vitamin D was indicated, it was with the drug and (acronym):
d. None of the above
The reference study in which a greater amount of vitamin D has been indicated, always in the form of cholecalciferol, was the Fracture Prevention Trial with Teriparatide, in which up to 1,200 IU of vitamin D.

3. In the reference study with zoledronate, we can affirm that it is true:
d. All of the above is true
In a study conducted on 153 women with postmenopausal osteoporosis who were to receive a first dose of zoledronate, it was observed that the levels of 25 - OH - vitamin D were lower in those who presented an acute phase reaction, so that those with 25 - OH - vitamin D levels <30 ng/ml presented 4.2 times the risk of presenting this reaction.

4. In the treatment of osteoporosis the administration of calcium and vitamin D is advised, since:
d. All of the above is true
It is advisable to correct the levels of calcium and vitamin D, preferably through diet or the use of supplements, in patients with osteoporosis who are going to receive an antiresorptive or osteoforming drug. It is a cost-effective intervention. In addition, the correction of vitamin D levels can be associated with a decrease in the risk of falls, and therefore with a lower risk of osteoporotic fractures.

5. Regarding the physiology of calcium and vitamin D, indicate the correct answer:
d. All of the above is true
The maximum bone mass is acquired by 30 years of age and depends on genetic and environmental factors, including calcium intake. Once the bone mass peak is achieved, it is necessary to maintain a minimum calcium intake to avoid bone loss. Vitamin D is responsible for maintaining calcium and phosphorus homeostasis, favoring its reabsorption at the renal and intestinal level. Its deficit is associated with an alteration of bone mineralization, causing rickets in children and osteomalacia in adults.

Role of calcium and vitamin D in the treatment of hip fracture patients

Olmos Martínez JM, Hernández Hernández JL

1. The most serious osteoporotic fracture is:
d. None of the above
The most serious osteoporotic fracture is the fracture of the proximal limb of the femur, also known as a hip fracture, due to its morbidity and its not negligible mortality.

2. The prevalence of vitamin D deficiency, defined as (serum levels of 25OHD <20 ng/ml) is very high in patients suffering from a hip fracture, reaching figures in Spain between:
d. 67-91%
The prevalence of hypovitaminosis D (serum levels of 25OHD <20 ng/ml) is very high in patients suffering from a hip fracture, reaching, for example, 36% in Finland, 40-68% in the United Kingdom, between 50-78% in the US, between 62-90% in Japan and between 67-91% in Spain.

3. The presence of a fracture implies an increased risk of fracture in subsequent years. In the specific case of the hip fracture, the incidence of refracture can reach:
b. 10%
The presence of a fracture implies an increased risk of fracture in subsequent years. On the other hand, the risk of fracture is especially important if the fracture is recent. In the specific case of hip fracture, the incidence of refracture can reach up to 10% during the first years.

4. In randomized studies it has been proven that the administration of vitamin D produces:
d. All of the above is true
Harwood et al. They observed that oral or parenteral vitamin D reduced the risk of falls after one year of presenting a hip fracture. Mak et al. They found that a single dose of cholecalciferol load (250,000 IU) followed by 800 IU daily, reduced the risk of falls compared to the isolated daily dose in 218 patients (77% women) followed for 26 weeks. Bishoff - Ferrari et al. They observed that the administration of high doses of vitamin D 2,000 IU/day to patients discharged after suffering a hip fracture reduced the rate of readmissions during the first year by up to 40%.

5. Point out the answer that seems false:
d. Pharmacological supplementation is preferable
Although there is no evidence of its effectiveness when administered in isolation, it is considered that calcium and vitamin D should be prescribed to every patient with osteoporosis, especially if they have suffered a fragility fracture. In our usual clinical practice, it is advisable that patients with hip fractures receive an adequate intake of vitamin D (daily dose between 800-1,000 IU), in addition to an appropriate amount of calcium (between 1,000-1,200 mg/day), this Last preferably with the diet.


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y del Metabolismo Mineral


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