Supplementation of vitamin D and calcium: advantages and risks*

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Calcium and the vitamin D hormonal system are both essential for the development and maintenance of skeletal health [1]. Calcium plays a vital role in neuromuscular function, many enzyme-mediated processes, blood clotting and in providing rigidity to the skeleton by virtue of its phosphate salts. Over 99% of the body’s calcium is stored in the bone, where, apart from providing mechanical strength, it serves as a mineral reservoir that can be drawn upon to maintain normal plasma calcium. Its non-structural roles require the strict maintenance of ionized calcium concentration in tissue fluids, at the expense of the skeleton if necessary, and therefore it is the skeleton which is at risk if the supply of calcium falls short of the requirement [1,2].

Calcium requirements are essentially determined by the relationship between absorptive efficiency and excretory rate—excretion being through the bowel, kidneys, skin, hair and nails. Absorbed calcium must match these obligatory losses, and the dietary intake must be large enough to ensure this rate of absorption if skeletal damage is to be avoided. The system is subject to considerable inter-individual variation in both calcium absorption and excretion for reasons that are not fully understood but which include vitamin D status, sodium and protein intake, age and menopausal status in women. A negative balance, even for short periods, is harmful because it takes so much longer to rebuild bone than to destroy it [1–3].

Vitamin D is required to maintain normal blood levels of calcium and phosphate, which are in turn needed for the normal mineralization of bone, muscle contraction, nerve conduction and the general cellular functioning of all body cells [1,3]. Vitamin D, derived from both endogenous (skin) and exogenous (diet) sources, is converted into 25OHD in the liver and then into 1,25(OH)2D in the kidneys. The latter metabolite controls calcium absorption. However, plasma 25OHD closely reflects vitamin D nutritional status, and because it is the substrate for the renal enzyme that produces 1,25(OH)2D, it could have mainly an indirect and also a direct effect on calcium absorption [4]. A vitamin D shortage would reduce the intestinal absorption of calcium, which could worsen if the diet is deficient of this element. In this scenario, there would be a tendency towards calcaemia decrease and the stimulation of parathyroid hormone (PTH) secretion, a secondary hyperparathyroidism, which has been described as one of the main pathogenic mechanisms of osteoporosis in the elderly [3,5] (Figure 1).

Osteoporosis and its clinical consequence, fragility fractures, are now recognized as major public health problems [6]. Bone mass declines and the risk of fractures increases as people age, especially post-menopausal women. An adequate intake of calcium and vitamin D, including supplementation, has been advocated as a universal primary intervention in the prevention and treatment of high-risk patients [1]. However, its efficacy in healthy post-menopausal women remains unclear [7]. In search of an answer to this question, the Women’s Health Initiative (WHI) examined the effect of calcium and vitamin D supplementation on the risk of fracture in 36 282 post-menopausal women between 50 and 79 years [8]. They were randomly assigned to receive a placebo or 1000 mg of elemental calcium plus 400 IU of vitamin D3 daily, and were followed up for an average of 7 years. Overall, calcium and vitamin D supplementation resulted in a small (1%) but significant improvement in hip bone density, and a trend, but insignificant, reduction (12%), in hip fractures. They did, however, show a 17% increase in the risk of developing kidney stones.

It should be highlighted that the women who took part in the study had an average daily intake of calcium and vitamin D, including allowed supplements of 1150 mg and 365 UI, respectively.
Likewise, the percentage of women with low bone mass and who showed new fractures was notably less than expected [9,10]. These facts indirectly indicate the overall good health of the whole cohort participating in the WHI study. Nevertheless, in subgroups of the study, such as those women over 60 years and those who adhered to the treatment, the reduction of the risk of fracture was significant; 21 and 29%, respectively. In addition, it should also be noted that 51% of participants, following protocol, received oestrogen and at least 10.7% received other bone antiresorptive drugs as well during the follow-up. It is important to mention that these two treatments might have influenced bone health and the final results, but unfortunately, these factors were not included in the adjustments of the study.

Calcium and vitamin D supplementation was safe, except for the increase in renal lithiasis incidence, which occurred with no apparent relation to the high-calcium basal intake. This finding differs from what was observed in the meta-analysis by Avenell et al. [7]; nevertheless, the WHI study based on number of persons and follow-up period was powerful enough to detect a low–moderate increased risk in nephrolithiasis. Furthermore, these results are ‘biologically congruent’ and partly in agreement with the results described in the young women cohort of the Nurses’ Health Study II [11], in which ‘a higher intake of dietary calcium decreases the risk of kidney stones, but supplemental calcium does not’.

What are the implications of the above findings for the clinician? First, not every person requires calcium and vitamin D supplementation. The recommendation for an adequate calcium and vitamin D intake as a universal measure for the prevention of bone and other diseases should be achieved through dietary measures and lifestyle. In spite of some minor remaining disagreements about the ‘recommended calcium and vitamin D intake and the desirable serum levels’ [2,12], the bulk of evidence shows that there is still a high proportion of people with inappropriately low calcium and vitamin D intake and serum levels [1,5,13]. For selective groups of people, such as the elderly (frequently older than 70 years), those with low solar exposure and in generally poor or inadequate nutritional condition, guaranteeing a daily intake of at least 1 g of calcium and 700–800 UI of vitamin D with supplements would have beneficial effects on bone health [7,14]. In such groups of people, the prevalence of low, moderate or even severe decrease of renal function (CKD2 to CKD4) is not infrequent [15–17]; accordingly, a vitamin D supplement should be given with the aim of reaching normal levels of calcidiol (around 30–40 ng/ml or 75—100 mmol/l) while keeping calcium intake between 1 and 1.5 g per day [16].

In those individuals with a high risk of osteoporotic fracture, calcium and vitamin D supplements are necessary but frequently insufficient, and so additional drugs may be required [18].

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References


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