PREVENTION OF FALLS AND FRACTURES - TO „D” OR NOT TO „D”?

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Two months ago JAMA published the new US Preventive Services Task Force (USPSTF) recommendations (1, 2) on vitamin D and calcium supplementation to prevent fall and fractures, and the evidence reports (3, 4).

Let us first shortly review the current knowledge. Falls in the elderly are an increasingly recognised public health problem, as almost a third of individuals over 65 years fall at least once a year, some are recurrent fallers and some falls are injurious leading to fractures. Most of the hip and non-vertebral fractures are following a fall and a high risk of falling is an important component of the imminent risk for fracture. A decade ago a new paradigm has evolved for preventing fractures by preventing falls (5,6). Supplementing with vitamin D elderly institutionalised people, where the prevalence of vitamin D deficiency is high, to decrease falls and fractures (7), is common practice. The problem comes with the use of supplementation in non-deficient community-dwelling adults, with and without osteoporosis. There is much confusion in the enormous literature published in the latest decades dedicated to this topic. The sources of the confusion are several: lack of standardization of serum 25OHD measurements; no universally accepted definition of sufficiency/deficiency; the concept of optimal concentration of 25 hydroxy-vitamin D (25OHD) (the more is better); the term vitamin D is a historical misnomer (6) as all the actions belong to active D (calcitriol) and are mediated by VDRs. Serum concentrations of 25OHD reflect exposure to this nutrient and not biological actions. Human muscle has VDRs in low concentration and is devoid of CYP27B1, and therefore in humans, as opposed to rodents, 25OHD is not a VDR ligand (8). Therefore escalating the dose of native vitamin D (2000 U/day and beyond) to get muscular benefits does not seem to be biologically sound. Moreover, a recent study points to the range between 21.2 to 30.4 ng/mL as optimal because both

25OHD concentrations below 21.2 ng/mL and above 44.5 ng/mL were associated with increased risk of falling (9). A further recent study observed increased faller rates as serum 25OHD exceeded 40-45ng/mL, arguing that higher doses of daily vitamin D3 increase falls (10).

Now, “USPSTF recommends against vitamin D supplementation to prevent falls in community-dwelling adults 65 years or older (D recommendation)” (2), based on evidence that vitamin D supplementation has no benefit in preventing falls in older adults (4). These recommendations apply to community-dwelling adults who are not known to have osteoporosis or vitamin D deficiency (2) and are in agreement with a well performed systematic review showing that vitamin D supplementation does not have a significant effect on muscle strength in vitamin D replete adults (11).

The USPSTF non-recommendation to use vitamin D is based on few studies, 5 with inconsistent results. Only 1 trial (calcitriol, 0.25 µg twice per day), showed a statistically significant reduction in falls and fallers but it was using active D (12). The well-known Australian trial with an annual high-dose (500.000 IU) which suggested increase in fall rate (13) included also patients with high risk for fracture and the median of serum 25OHD was only 21 ng/mL, and therefore included an unknown proportion of deficient individuals. Anyway, removing this study from analyses no statistically significant association between vitamin D and falls was found.

The USPSTF “recommends exercise interventions to prevent falls in community-dwelling adults 65 years or older who are at increased risk for falls (B recommendation)” (2), confirming a 2017 meta-analysis of falls prevention interventions (14). Identifying persons at high risk for falls is not yet standardized also, and clinicians rely on a history of falls or use tests of global performance as Timed Up and Go, chair rising, and others.

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Therefore what's new? The current review excluded studies with vitamin D deficiency or insufficiency and is more focused on fall endpoints, like incident falls, not only number of fallers, and on the remaining evidence is not recommending supplementations with vitamin D (and calcium) for fall prevention in older healthy individuals.

Regarding the other topic of the new release, namely the supplementation with calcium and vitamin D for primary fracture prevention, there nothing new as USPSTF maintains the 2013 recommendation. The USPSTF "recommends against daily supplementation with 400 IU or less of vitamin D and 1000 mg or less of calcium for the primary prevention of fractures in community-dwelling, postmenopausal women (D recommendation)"(1). At the same time USPSTF acknowledges that "recommendations do not apply to persons with a history of osteoporotic fractures, increased risk for falls, or a diagnosis of osteoporosis or vitamin D deficiency"(1). Regarding the supplementation with higher doses of vitamin D, the USPSTF concluded that "the current evidence is insufficient to assess the balance of the benefits and harms" for primary prevention of fractures in community-dwelling, postmenopausal women (I statement) (1). This is a little bit confusing; actually these recommendations are addressed to healthy older people for primary prevention of fracture and the vitamin D dose should be not less than 400 IU a day. A word of caution is also to be added as in the real life the adherence to calcium and vitamin D supplementation is low and this preventive action should be part of other healthy recommendations (15). On the other side, the USPSTF "found sufficient evidence that supplementation with calcium and vitamin D increases the risk of kidney stones"(1), but "identified no clear evidence for an increased risk of cardiovascular disease with vitamin D alone"(3) confirming previous meta-analyses and the results of a 2018 very large prospective cohort (16). The relationship between the dose of both nutrients and the risk of incident kidney stones was not evaluated.

A quite recent Mendelian randomization study does not support a causal association between long-term higher average serum 25OHD, concentrations and bone mineral density (BMD) in generally healthy populations (17), which is not in favor of vitamin D supplementation.

It is important for the clinicians and patients to understand that these recommendations are not intended to change the current management of osteoporosis, where supplementing with calcium and

vitamin D is current practice. Similarly, almost all international guidelines recommended calcium and vitamin D supplementation for target groups (elderly population at high risk of vitamin D deficiency such as the institutionalized elderly subjects or the 'oldest old' or other similar risk groups) (18). Therefore, for patients at increased risk for osteoporosis, those with vitamin D deficiency, or both, it remains reasonable to consider vitamin D supplementation.

Major institutions, like National Osteoporosis Foundation, the Institute of Medicine, The Endocrine Society and almost all national clinical guidelines recommend supplementation of older women and men with calcium and vitamin D (800-1000 IU daily) for the prevention of falls and fractures, mostly as an adjunct to bone-protective therapy for osteoporosis (19-21), as well as for other reasons unrelated to calcium-phosphate metabolism (22, 23).

The current evidence will soon be expanded as some large double-blind randomized clinical trials on vitamin D supplementation among community-dwelling adults will have their results published (24).

Conflict of interest

The authors declare that they have no conflict of interest.

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