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LETTER

Vitamin D supplementation and fracture risk in adults: a new insight

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Dear Editor,

An excellent review by Reid and Bolland [1] properly highlights an appropriate dose of vitamin D supplementation on the basis of experimental and clinical data; importantly, higher levels of vitamin D can stimulate bone resorption and inhibit bone mineralization [2]. Here, we would like to discuss this topic from a different point of view, i.e. skeletal adaptation to mechanical environment.

The latest evidence includes two noteworthy findings. First, detailed analyses using human bones [3] showed that vitamin D deficiency impaired bone quality at multiple scales, independently of areal bone mineral density (BMD). Second, a meta-analysis [4] found that the effects of daily supplementation with 800 IU or more of vitamin D on areal BMD were lower than that with less than 800 IU of vitamin D in the lumbar spine (−0.1 % vs. 0.4 %, $p=0.04$) and potentially in the femoral neck (0.3 % vs. 1.4 %, $p=0.06$), but not in the forearm (−0.3 % vs. −0.3 %, $p>0.9$).

The skeleton normally adapts to mechanical stimulation through the control of bone strength by resulting elastic deformation (strain) of bone, and a hypothesis has proposed that the effect of osteoporosis therapy is limited by such natural homeostatic system because increased bone strength results in decreased bone strain from mechanical loading [5]. Skeletal fragility is associated with bone quantity (areal BMD) and quality and, if higher doses of vitamin D supplementation contribute to bone strength by increasing bone quality [3], the feedback control system [5] would cause the compensatory negative effect on areal BMD to maintain the adapted strain level at the weight-bearing sites (lumbar spine and femoral neck) but not the non-weight-bearing site (forearm) [4].

Consistent with the conclusion by the Institute of Medicine, a trial sequential meta-analysis found that vitamin D supplements did not decrease falls by 15 % or more [6]. Skeletal adaptation to mechanical loading implies that higher doses of vitamin D supplementation would be unlikely to significantly improve muscle function associated with an increase in daily mechanical loads because of their less effect on areal BMD [4].

The above logic is compatible with recent consistent results indicating that vitamin D supplementation alone (without calcium) does not significantly reduce fracture risk in adults without vitamin D deficiency [7–9], although appropriate vitamin D is essential for bone health [10].

Finally, a population-based cohort study reported that areal BMD in the femoral neck was positively associated with circulating levels of 25-hydroxyvitamin D in white, but not black, Americans [11]. The former association is inconsistent with the less effect of higher doses of vitamin D supplementation on areal BMD [4], suggesting that mechanical loading from physical activity, rather than circulating levels of 25-hydroxyvitamin D, is directly related to areal BMD because black Americans would have less vitamin D synthesis in the skin after sunlight exposure that is linked to outside activity. If correct, the association in white Americans [11] might be the result of physical activity with sunlight exposure; the low levels of 25-hydroxyvitamin D could be a marker of ill health [12].

Conflicts of interest None.

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