BONE

Vitamin D deficiency implicated in bone mineralization defects

Bone mineralization defects might be prevalent in otherwise healthy individuals with low 25-hydroxyvitamin D levels, according to a report published in the *Journal of Bone and Mineral Research*. “Our data demonstrate that defects of bone mineralization occur in patients with serum 25-hydroxyvitamin D levels below 75 nmol/l and strongly argue that levels of 25-hydroxyvitamin D should reach this minimum threshold to maintain skeletal health,” states lead researcher Michael Amling of the University Medical Center Hamburg-Eppendorf, Germany.

No consensus currently exists as to the minimum serum concentration of 25-hydroxyvitamin D necessary to guarantee skeletal health. Seasonal and geographic fluctuations in the levels of 25-hydroxyvitamin D are reported; these variations relate to levels of exposure to ultraviolet light (a key determinant in the vitamin D synthetic pathway) and dietary intake of vitamin D. To further complicate matters, parathyroid hormone is commonly used as a surrogate measure of vitamin D status.

Priemel and colleagues postulated that histomorphometric assessment of bone quality might provide a more direct approach to the evaluation of vitamin D status than measurement of serum parathyroid levels. To test their hypothesis, the researchers examined a group of individuals from northern Germany, who had no pre-existing bone disease or conditions likely to affect bone mineralization (for example, renal failure or cancer). As vitamin D deficiency is endemic in Germany—a consequence of low levels of sunlight, coupled with a government-led, public-health policy that prohibits fortification of foodstuffs with vitamin D—this cohort represents an ideal sample in which to study the relationship between vitamin D status and bone mineralization.

Priemel *et al.* obtained blood and transiliac crest biopsy specimens from

675 individuals (age range 20–100 years) at autopsy; causes of death were not illness-related and included motor vehicle accident, assault and suicide. The autopsy results allowed the researchers to rule individuals with primary or secondary bone disease out of the subsequent analysis. The primary outcome measures of the study were the serum levels of 25-hydroxyvitamin D and histomorphometric indices of skeletal mineralization (bone volume, trabecular number, trabecular thickness, trabecular separation, osteoid volume and osteoid surface).

The investigators found that an appreciable number of the bone biopsy specimens displayed bone mineralization defects (defined as an osteoid volume >2%): 25.63% of the samples examined had an osteoid volume of up to 17.44%. As expected, vitamin D deficiency was prevalent among the study cohort. Of note, however, pathologic defects of bone mineralization were only detected among individuals whose serum 25-hydroxyvitamin D level was <75 nmol/l. Priemel *et al.* conclude that this level of 25-hydroxyvitamin D should be considered the minimum target to maintain bone health.

The findings reported by Priemel and co-workers have direct implications for the treatment of osteoporosis. Randomized, controlled trials of anti-osteoporotic agents have so far been conducted in the context of adequate vitamin D supplementation. As a result, little data exists as to the efficacy of these agents in patients with vitamin D deficiency. “On a background of endemic vitamin D deficiency (such as is found in Germany), it is tempting to speculate that even the patients receiving specific osteoporosis treatment do not benefit in an optimal way in regard to fracture prevention,” Amling comments.

The next step for Amling and his team is to expand the number of individuals included in the study cohort and perform

subgroup analyzes. In addition, the group plan to evaluate the relationship between serum 25-hydroxyvitamin D concentration and additional measures of bone quality, such as distribution of BMD. A key goal is to persuade the German government to rethink its policy on food fortification. “We have already done a health-economic Markov analysis,” Amling explains, “our results show that a population-wide daily supplementation with vitamin D would save the German health care system around 2.5 billion euros annually, and prevent some 25,000 hip fractures every year.”

Vicky Heath

Original article Priemel, M. *et al.* Bone mineralization defects and vitamin D deficiency: histomorphometric analysis of iliac crest bone biopsies and circulating 25-hydroxyvitamin D in 675 patients. *J. Bone Miner. Res.* doi:10.1359/jbmr.090.728